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Sponsor:

Dynamac Corporation
11140 Rockville Pike
Rockville, Maryland 20852

FINAL REPORT

Study Title:

Subchronic Toxicity Study in Rats
with m-Xylene

Author:

Gary W. Wolfe, Ph.D., D.A.B.T.

Performing Laboratory:

Hazleton Laboratories America, Inc.
1330-B Piccard Drive
Rockville, Maryland 20850-4373

Laboratory Project Identification:

HLA Study No. 2399-108

May 27, 1988

PROTOCOL AMENDMENT



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PROJECT NO. 2399-108 AMENDMENT NO. 2 DATE EFFECTIVE: 6/30/86

PROJECT NO. 1000-1
STUDY TITLE: Subchronic Toxicity Study in Rats with m-Xylene

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Date and Means of Sponsor Authorization (if appropriate):

Amendment:

1. Page 4, 11.C. (4) (a): Samples of the lowest and highest levels will be analyzed for stability.

Reason: Changed to agree with Attachment #3 (page 16), "Stability".

2. Page 7, 11.F. (2): Animals will be killed by exsanguination under sodium pentobarbital anesthesia.

Reason: Requested by Sponsor.

3. Page 7, 11.G. (2): Organ weights will not be recorded for those animals selected for electron microscopy.

Reason: Because of whole-body infusion, weights would not be comparable.

4. Page 7, 11.G. (2): Testes will be weighed with epididymis.

Reason: Not previously specified.

5. Page 8, 11.G. (3): Electron microscopy will be performed on 5 animals/sex in the control group and 10 animals/sex in all treated groups.

Reason: Requested by Sponsor.

STUDY DIRECTOR:

DATE:

PROTOCOL AMENDMENT



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PROJECT NO. 2399-108 AMENDMENT NO. 3 DATE EFFECTIVE: 8/5/86

STUDY TITLE: Subchronic Toxicity Study in Rats with m-Xylene

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Toxicology (2)

Pathology (3)

Analytical Chemistry (1)

* Unless otherwise directed.

Date and Means of Sponsor Authorization (if appropriate):

Amendment:

Due to scheduling difficulties, the interim bloodwork was performed during Week 5 rather than Week 4.

STUDY DIRECTOR: Gay W. Wolfe

DATE: 8/5/86



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- 2 -

COMPLIANCE STATEMENT
Subchronic Toxicity Study in Rats with m-Xylene

This study was conducted in compliance with the Good Laboratory Practice Regulations as set forth in Title 40 of the U.S. Code of Federal Regulations Part 160. There are no significant deviations from the aforementioned regulations which affected the quality or integrity of the study or the interpretation of the results in the report.

Study Director:

Gary W. Wolfe 5/27/78
Gary W. Wolfe, Ph.D., D.A.B.T. Date
Life Sciences Division



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- 3 -

QUALITY ASSURANCE UNIT**Project Title:** Subchronic Toxicity Study in Rats with m-Xylene**Project No.:** 2399-108

Quality Assurance Review of the final report was conducted according to the procedures described in the standard operating procedures of the Report Review Section of the Quality Assurance Unit, and according to the general requirements of the Good Laboratory Practice Regulations issued by the Environmental Protection Agency for compliance on or after May 2, 1984. The final report review was conducted and the findings were reported to management and to the study director on the following dates:

<u>Final Report Review</u>	<u>Findings Reported</u>	<u>Reviewer</u>
Protocol 4/10/86	4/10/86	D. Goldsteen
Inspection 1 4/22, 24/86	5/9/86	D. Goldsteen
Inspection 2 9/2, 7, 8/86	7/15/86	D. Goldsteen
Final Report 8/28, 29; 9/2-5/86	9/9/86	K. Glenn
12/2/86	12/8/86	K. Reilly
5/26, 27/88	5/27/88	E. Jenkins


Final Report Reviewer
Quality Assurance Unit

5/31/88
Date Released





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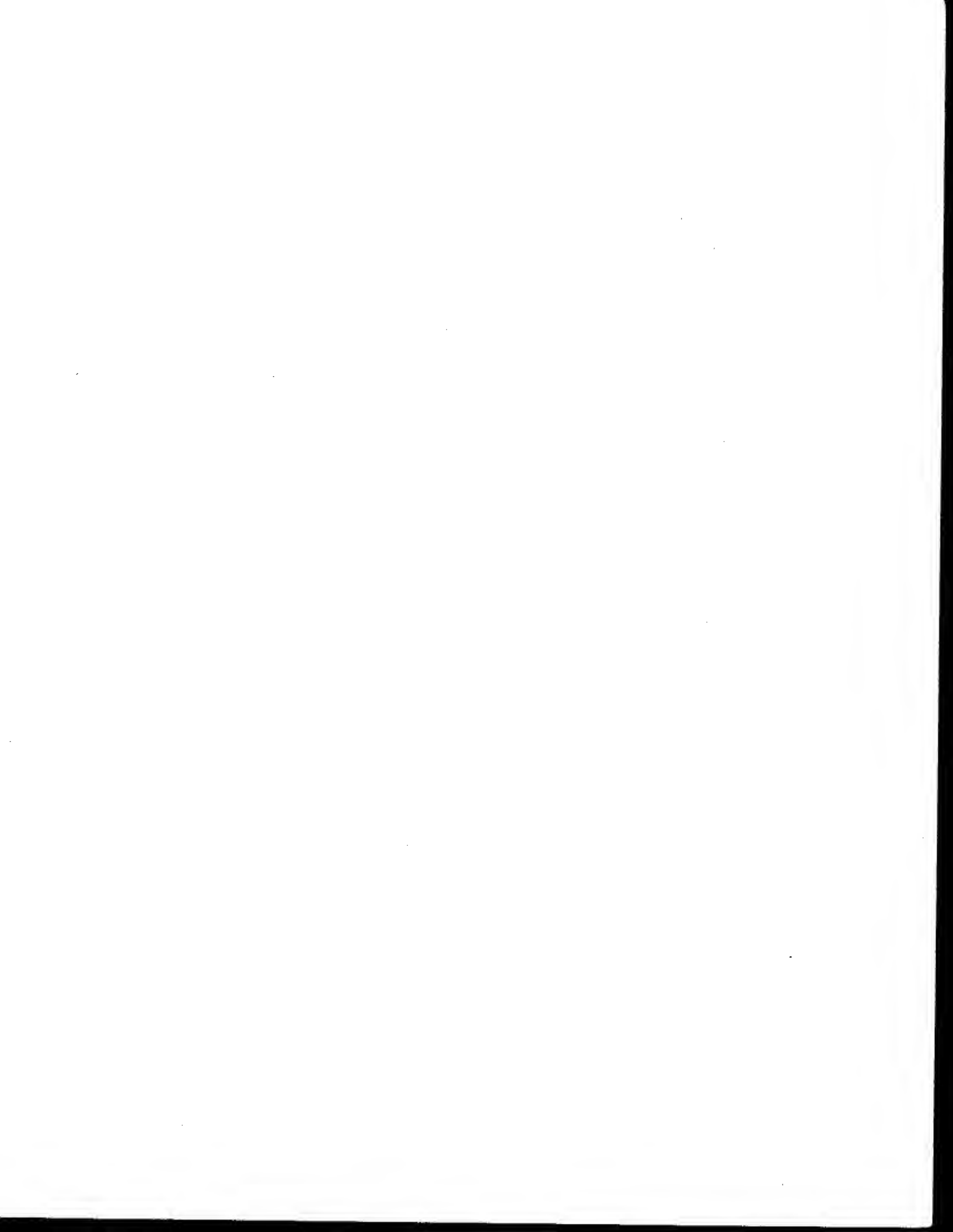
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- 4 -

STUDY IDENTIFICATION
Subchronic Toxicity Study in Rats with m-Xylene

HLA Study Number	2399-108
Test Material	m-Xylene (CAS 108-38-3)
Sponsor/Study Monitor	Sharon Segal, Ph.D. Dynamac Corporation 11140 Rockville Pike Rockville, Maryland 20852 (301) 468-2500
Study Director	Gary W. Wolfe, Ph.D., D.A.B.T. Hazleton Laboratories America, Inc. 1330-B Piccard Drive Rockville, Maryland 20850-4373 (301) 670-9600
Study Timetable	
Initiation Date	April 11, 1986
Termination Date	July 16, 1986



- 5 -

STUDY PERSONNEL
Subchronic Toxicity Study in Rats with m-Xylene

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Veterinarian:	Joseph A. Manda, III, D.V.M., M.S.
Pathologist:	Borge M. Ulland, D.V.M.
Statistician:	Ajit K. Thakur, Ph.D.
Analytical Chemist:	Susan A. Lewis, Ph.D.
Laboratory Supervisor:	Preston Burlew, B.A.



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HLA 2399-108

- 6 -

CONTENTS

	<u>Page</u>
SUMMARY -----	8
INTRODUCTION -----	9
TEST MATERIAL -----	9
TEST ANIMALS -----	9
METHODS -----	10
Groups and Dose Levels -----	10
Compound Preparation and Administration -----	10
Analytical Chemistry -----	11
Observations and Records -----	11
Ophthalmoscopic Examinations -----	11
Clinical Pathology -----	11
Sacrifice and Gross Pathology -----	12
Organ Weights -----	13
Tissue Preservation -----	13
Histopathology -----	13
Statistical Analysis -----	14
Raw Data and Final Report Storage -----	15
RESULTS -----	17
Mortality -----	17
Clinical Signs -----	17
Body Weights and Food Consumption -----	17
Ophthalmoscopic Examinations -----	18
Clinical Pathology -----	18
Organ Weights and Organ-to-Body Weight Ratios -----	21
Gross Pathology -----	21
Histopathology -----	21
Analytical Chemistry -----	22
DISCUSSION -----	23
PATHOLOGY SUMMARY -----	25

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HLA 2399-108

- 7 -

CONTENTS (Continued)

	<u>Page</u>
FIGURES	
1 - Flowchart of Anova and Related Methods -----	16
2 - Mean Body Weight Plots -----	19
3 - Mean Food Consumption Plots -----	20
REFERENCES -----	
	27
TABLES	
1 - Adjusted Survival -----	33
2 - Summary Incidence of Clinical Signs -----	34
3 - Incidence of Daily Observations -----	35
4A - Mean Body Weights and Standard Deviations -----	39
4B - Mean Body Weight Changes -----	40
5A - Mean Food Consumption and Standard Deviations -----	41
5B - Mean Total Food Consumption and Standard Deviations -----	42
6 - Mean Clinical Hematology Values -----	43
7 - Mean Clinical Chemistry Values -----	48
8 - Absolute Organ Weight Means -----	53
9 - Organ-to-Terminal Body Weight Ratio Means -----	55
10A - Gross Pathology Incidence Summary - Terminal Sacrifice --	57
10B - Gross Pathology Incidence Summary - Unscheduled Deaths --	64
11A - Histopathology Incidence Summary - Terminal Sacrifice --	71
11B - Histopathology Incidence Summary - Unscheduled Deaths --	78
APPENDICES	
1 - Individual Animal Disposition -----	86
2 - Individual Clinical Observations -----	91
3 - Individual Body Weights -----	95
4 - Individual Food Consumption -----	100
5 - Individual Ophthalmoscopic Findings -----	105
6 - Individual Clinical Hematology Values -----	109
7 - Individual Clinical Chemistry Values -----	141
8 - Individual Animal Summary Report -----	163
9 - Analytical Chemistry Report -----	386
10 - Study Protocol and Amendments -----	431



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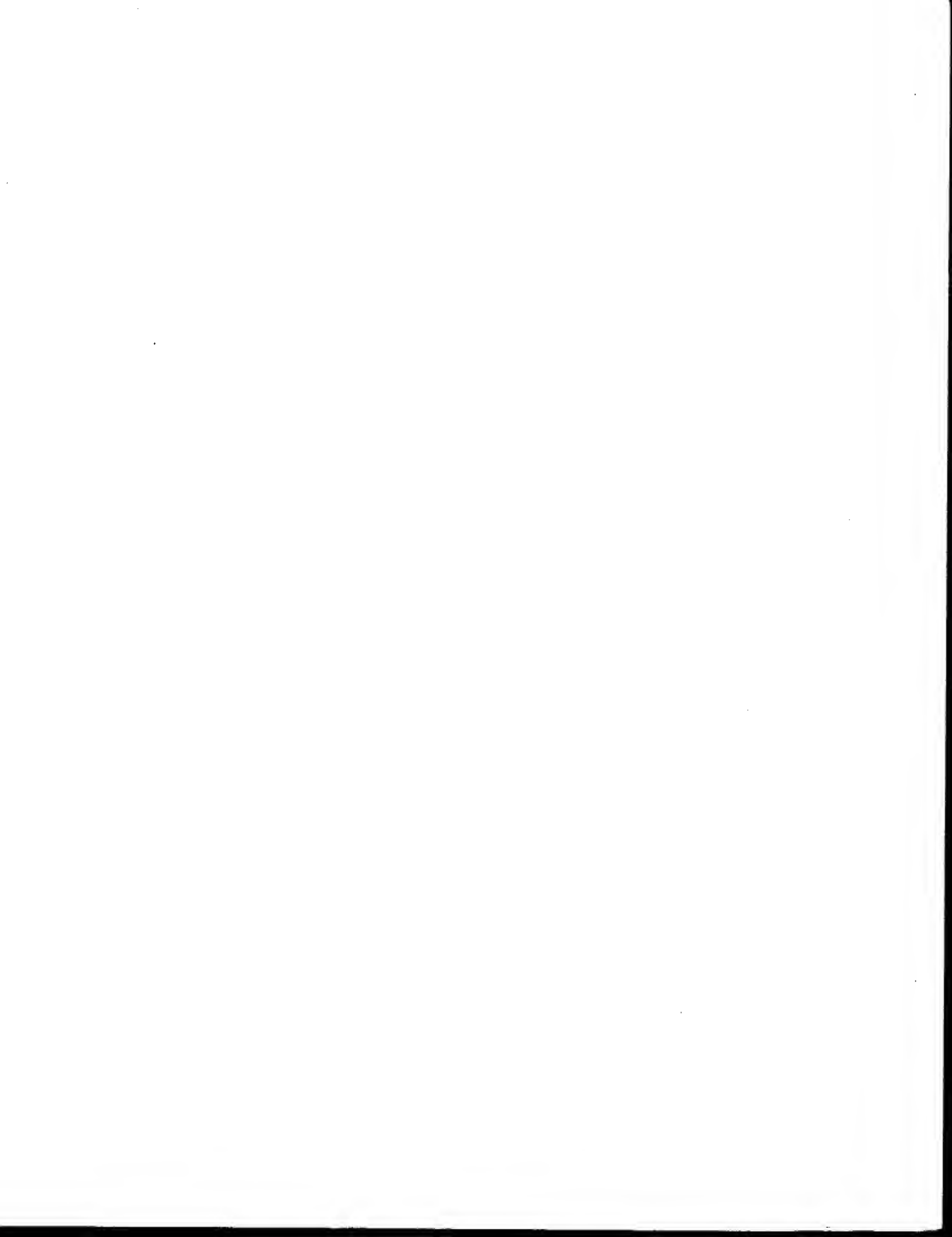
- 8 -

SUMMARY

The test material, m-Xylene (CAS 108-38-3), was administered to male and female rats by oral gavage in order to evaluate its subchronic toxicity. Dose levels were 0, 100, 200, and 800 mg/kg/day (Groups 1 through 4, respectively), with 20 animals/sex/group dosed daily for at least 90 days. Criteria evaluated included mortality, clinical signs, body weights, food consumption, ophthalmologic examinations, hematology, clinical chemistry, organ weights, organ-to-body weight ratios, gross pathology, and histopathology.

Mortality was significantly increased in male Group 3 and female Groups 3 and 4; however, based on histopathology findings, these deaths were most likely the result of vehicle and/or compound aspiration. Salivation was frequently observed in both sexes of Group 4 and only rarely in the other treated groups. Total body weight gain was significantly decreased in male Groups 3 and 4, and female Group 4. Food consumption was significantly decreased from Week 1 to 5 in Group 4 males and from Week 6 to 9 in Groups 3 and 4 males. A few clinical pathology parameters were significantly increased or decreased and with one exception (female Group 3), all were in Group 4. A few significant changes were seen in absolute or relative organ weights, all of which were in male Group 4. The most commonly observed lesions at necropsy were in the lungs (mottled and failure to collapse). These lesions were only seen in the animals found dead. No apparent compound-related effects were present in the ophthalmology or histopathology findings.

Based on the results of this study, with the assumption that the decrease in survival was the result of vehicle and/or compound aspiration, the no-observed-effect level (NOEL) of m-Xylene was 200 mg/kg/day in the females. However, due to significantly decreased body weight gain in Groups 3 and 4, the NOEL for the males was 100 mg/kg/day.



- 9 -

INTRODUCTION

The purpose of this study was to evaluate the subchronic toxicity of m-Xylene when administered to rats daily by oral gavage for at least 90 days. The study was conducted according to applicable EPA guidelines and the Good Laboratory Practice regulations.

A copy of the study protocol and all amendments are contained in Appendix 9. The study was initiated on April 11, 1986, and was terminated on July 16, 1987. The study was performed at the Rockville, Maryland, facility of Hazleton Laboratories America, Inc. (HLA).

TEST MATERIAL

The test material, m-Xylene (CAS 108-38-3), Lot No. 259 211, was a clear, colorless liquid. It was received from Fluka Chemical Corporation, Hauppauge, New York, in three shipments (March 6, April 17, and April 30, 1986) and was stored frozen and protected from light. Dosing formulations were prepared using corn oil as the vehicle and were adjusted to 100% activity, based on a purity of 99%. The formulated test material was stored at room temperature.

Analyses for purity, stability, and dose concentration were performed on the test material.

TEST ANIMALS

Sprague-Dawley rats were used in this study because they have historically been used in safety evaluation studies and were requested by the EPA. A total of 168 males and 168 females was received from Charles River Breeding Laboratories, Inc., Portage, Michigan, on March 25, 1986. They were acclimated to laboratory conditions for approximately two weeks, making them 46 days of age at the time of study initiation. The body weights at initiation ranged from 203.7 to 246.4 g for the males and 142.1 to 174.8 g for the females.

- 10 -

The rats were uniquely identified by ear tags and cage cards and were housed individually in elevated wire-mesh cages. Commercial rodent diet (Purina Certified Rodent Chow® #5002) and acidified tap water were available ad libitum. The temperature and relative humidity in the animal room were recorded twice daily (with few exceptions) and ranged from 70 to 77°F and 31 to 69%, respectively. A 12-hour light/dark cycle was maintained daily via artificial illumination.

METHODS

Groups and Dose Levels

Following physical and ophthalmologic examinations, 85 clinically acceptable rats of each sex were assigned to treatment groups (shown below) using a computer weight randomization program. Animals not selected were assigned to another study or discarded without necropsy. Baseline groups were used for pretreatment bloodwork and later discarded without necropsy.

Group	No. of Animals		Animal Numbers		Dose Level (mg/kg/day)
	Males	Females	Males	Females	
1 (Control)	20	20	8362-8381	8382-8401	0
2	20	20	8402-8421	8422-8441	100
3	20	20	8442-8461	8462-8481	200
4	20	20	8482-8501	8502-8521	800
5 (Baseline)	5	5	8522-8526	8527-8531	0

Compound Preparation and Administration

Dosing solutions were prepared weekly according to the following procedure. For each dose level, the calculated amount of test material was weighed and transferred to a volumetric flask. Corn oil was added to achieve the final volume, then the flask was capped and inverted by hand until thoroughly mixed.

The formulated test material was administered to the animals by oral gavage daily for 13 weeks; control animals received the vehicle only. The dosing factor was 2.5 mL/kg.

- 11 -

Analytical Chemistry

The test material was analyzed for identity and purity prior to initiation of the study and again at termination for purity only. Formulated test material was analyzed for stability and dose concentration. The schedule and results of these analyses are included in the Analytical Chemistry Report (Appendix 9).

Observations and Records

All rats were observed for overt signs of toxicity daily, beginning about one hour after completion of dosing. In addition, a cursory exam was conducted during dosing. Complete physical examinations were performed at initiation and weekly thereafter. Mortality/moribundity checks were performed twice daily. Individual body weights were recorded during the randomization procedure, at initiation, and weekly thereafter. Food consumption was recorded weekly.

Ophthalmoscopic Examinations

Ophthalmoscopic examinations were performed by a board-certified veterinary ophthalmologist on all animals to be used on study prior to treatment and on the last ten survivors per sex per group during Week 13. Pupils of both eyes were dilated prior to examination using 1% Atropine Sulfate.

Clinical Pathology

Clinical pathology determinations (shown below) were made on five animals per sex (Baseline group) prior to initiation and on the first ten survivors per sex per group during Weeks 5^a and 13. Following an overnight fast, samples were collected via the orbital sinus while under carbon dioxide anesthesia.

^aProtocol required bloodwork for Week 4 was actually performed during Week 5.



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- 12 -

Hematology:

leukocyte count
erythrocyte count
hemoglobin
hematocrit

platelet count
differential leukocyte count
reticulocyte count
cell morphology

Serum Chemistry:

sodium
potassium
chloride
total protein
albumin
calcium
phosphorus
total bilirubin
urea nitrogen

creatinine
glucose
SGOT/AST
SGPT/ALT
globulin
alkaline phosphatase
cholesterol
albumin/globulin ratio
lactate dehydrogenase

Sacrifice and Gross Pathology

All animals that died during the course of the study and all survivors sacrificed after 13 weeks of treatment were given a complete gross necropsy. The method of euthanasia was exsanguination while under sodium pentobarbital anesthesia. The necropsy included examination of the following:

- the external surface
- all orifices
- cranial cavity
- carcass
- external surface of the brain
- the thoracic, abdominal, and pelvic cavities and their viscera
- the tissues and organs of the neck region

At the terminal sacrifice, five animals per sex from the control group and 10 animals per sex from each treated group were selected for electron microscopy. A separate report, including methods and results, is to be submitted to the Sponsor by the performing laboratory.

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- 13 -

Organ Weights

For all terminally killed animals, except those selected for electron microscopy, the following organs were weighed. Organ-to-body weight ratios were calculated using each animal's terminal body weight.

liver
kidneys
spleen
adrenal glands

brain with stem
heart
testes with epididymides
ovaries

Tissue Preservation

The following tissues from each animal (when present) were preserved in 10% neutral buffered formalin:

all gross lesions
brain with brainstem
(medulla/pons, cerebellar cortex, and cerebral cortex)
pituitary
thyroid with parathyroids
thymus
lungs
trachea
heart
salivary glands (mandibular)
liver
sternum with bone marrow
mammary gland
thigh musculature
eyes
skin
epididymides
prostate
seminal vesicles

kidneys
adrenals
pancreas
testes
ovaries
uterus
spleen
aorta
esophagus
stomach (forestomach and glandular)
duodenum, jejunum, ileum
colon, cecum, rectum
urinary bladder
mesenteric lymph node
sciatic nerve
femur including articular surface
cervical spinal cord
mid-thoracic spinal cord
lumbar spinal cord
exorbital lacrimal glands

Histopathology

All preserved tissues from all animals were embedded in paraffin, sectioned, and stained with hematoxylin and eosin.



- 14 -

The following tissues were examined microscopically:

- (1) All tissues from control and high-dose animals and from all animals not surviving to termination.
- (2) Gross lesions, lungs, liver, and kidneys from all remaining animals.

Statistical Analysis

Cumulative survival data were analyzed using the National Cancer Institute Package (Life Table Analysis). Trend analysis of survival was evaluated at the 5.0% one-tailed probability level.

Body weights, food consumption, appropriate clinical pathology data, and organ weight data from the control group were compared to those of the treated groups of the same sex. Tests for homogeneity of variances and ANOVA were evaluated at the 5.0% one-tailed probability level. Control vs. treated group means were evaluated using Dunnett's t-test at the 5.0% two-tailed probability level.

Data transformations were performed when variances were heterogeneous (see Figure 1) and are indicated in the tables by the appropriate superscript next to the control group mean:

A = Data analyzed following \log_{10} transformation

B = Data analyzed following square (x^2) transformation

C = Data analyzed following square root ($x^{1/2}$) transformation

D = Data analyzed following reciprocal ($1/x$) transformation

E = Data analyzed following angular (arcsine $x^{1/2}$) transformation

F = Data analyzed following rank transformation



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- 15 -

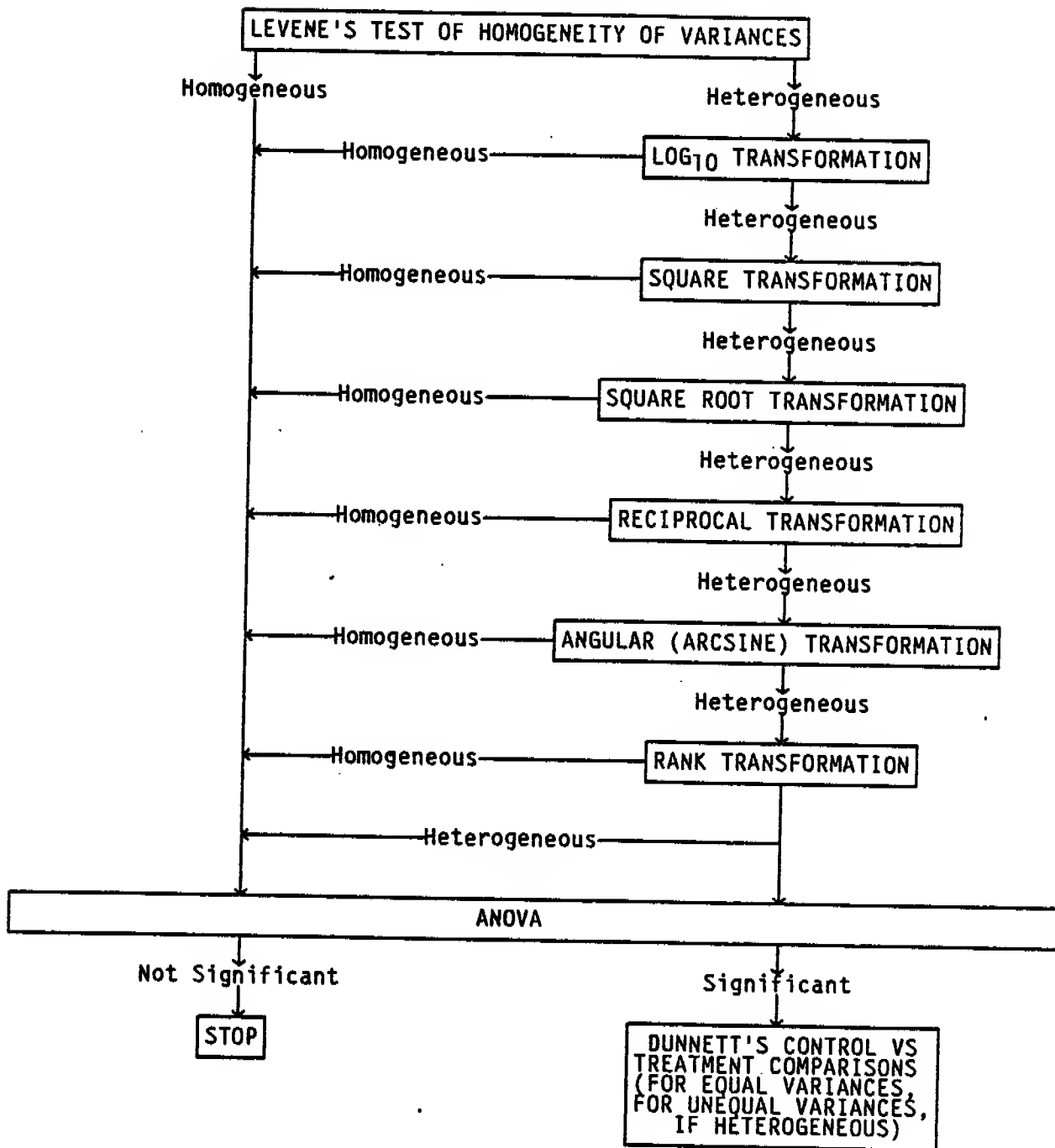
Throughout this report, when an effect is referred to as "significant", it means there is a statistically significant difference between the control group and the specified treated group of the same sex. Statistical significance is indicated in the tables by an "s" superscript next to the treated group mean.

Raw Data and Final Report Storage

All raw data and the final report are stored in the archives of Hazleton Laboratories America, Inc.

FIGURE 1

FLOWCHART OF ANOVA AND RELATED METHODS





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- 17 -

RESULTS

Mortality

Group survival data, by week of study, are presented in Table 1. Individual animal disposition is presented in Appendix 1.

In the males, there was significantly higher mortality in Group 3, but there was not a significant trend. In the females, there was significantly higher mortality in Groups 3 and 4 and there was a significant trend.

Clinical Signs

A summary incidence of weekly clinical signs is presented in Table 2; individual data are presented in Appendix 2. A summary incidence of daily observations is presented in Table 3 (signs with only a single occurrence are not included).

The most commonly observed weekly clinical signs were chromodacryorrhea, malocclusion, and urine stains. Of the signs recorded, only urine stains showed a possible relationship to treatment: it was seen only in both sexes of Group 4.

Daily observations included hyperactivity, convulsions, salivation, and epistaxis. Except for salivation, these were observed only during the first three weeks of the study and with low frequency. Salivation was observed in both sexes of Group 4 during almost every study week, with the incidence considerably higher in the females. Generally, salivation was observed just prior to dosing and the animals were back to normal by the one-hour post-dosing observations.

Body Weights and Food Consumption

Mean body weights are presented in Tables 4A (Mean Body Weights), 4B (Body Weight Change) and graphically in Figure 2; individual values are

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- 18 -

presented in Appendix 3. Food consumption data are presented in Tables 5A (Weekly Mean Values), 5B (Total Food Consumption at Selected Intervals) and graphically in Figure 3; individual values are presented in Appendix 4.

The mean body weight gain over the course of the study was significantly decreased in Groups 3 and 4 of the males and in Group 4 of the females. The body weight curves in Figure 2 show a clear relationship between dose and body weight depression in both sexes.

Statistical analyses were performed on food consumption data for three intervals: Weeks 1-5, 6-9, and 10-13. Food consumption was significantly decreased from Weeks 1 to 5 in the Group 4 males and from Weeks 6 to 9 in the Groups 3 and 4 males. Food consumption data among the female groups was comparable at all three intervals.

Ophthalmoscopic Examinations

Individual ophthalmoscopic findings and copies of the ophthalmologist's reports are presented in Appendix 5.

Only two animals (one Group 1 male and one Group 3 male) showed abnormalities at the terminal examination. These were judged to be unrelated to treatment.

Clinical Pathology

Mean hematology values are presented in Table 6; individual values are presented in Appendix 6. Mean clinical chemistry values are presented in Table 7; individual values are presented in Appendix 7.

At the Week 5 interval, only one hematology parameter was significantly different: hematocrit was decreased in Group 4 females. At Week 13, there were no significant changes in the hematology values of either sex.

There were significant changes in a few of the clinical chemistry parameters at the Week 5 interval. In Group 4 males, potassium was increased and total bilirubin was decreased. In the females, cholesterol and calcium

FIGURE 3 - MEAN FOOD CONSUMPTION

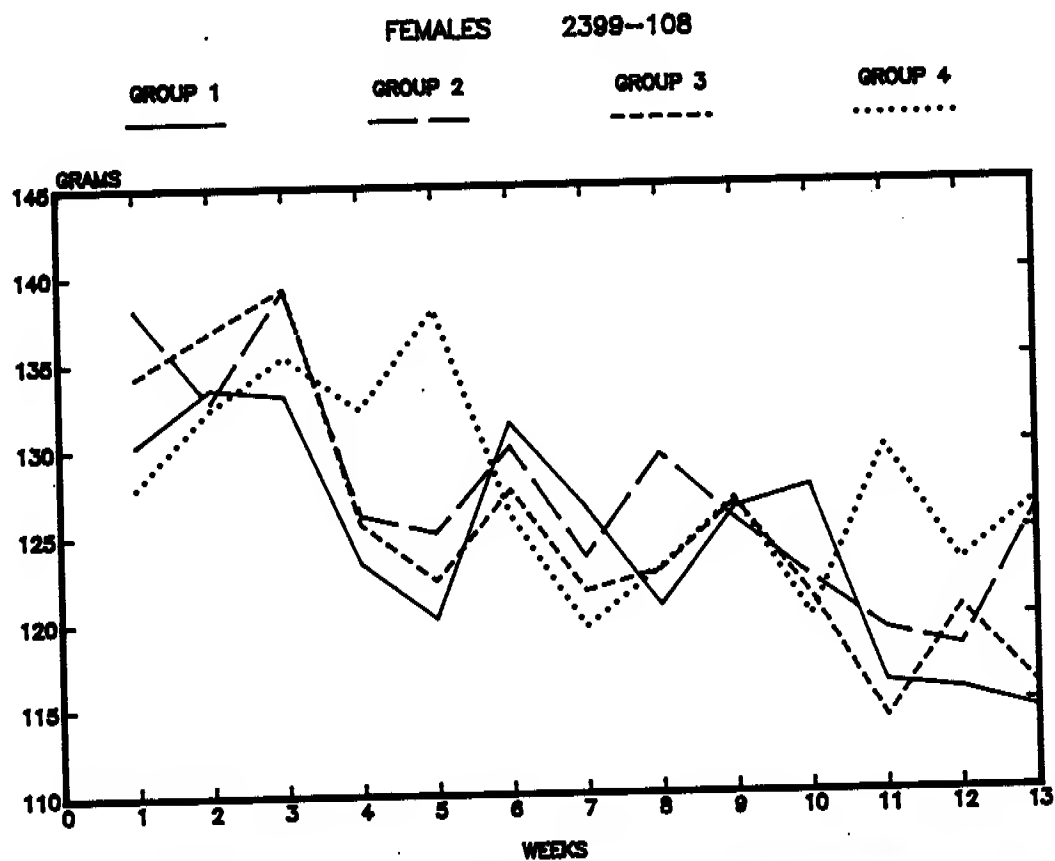
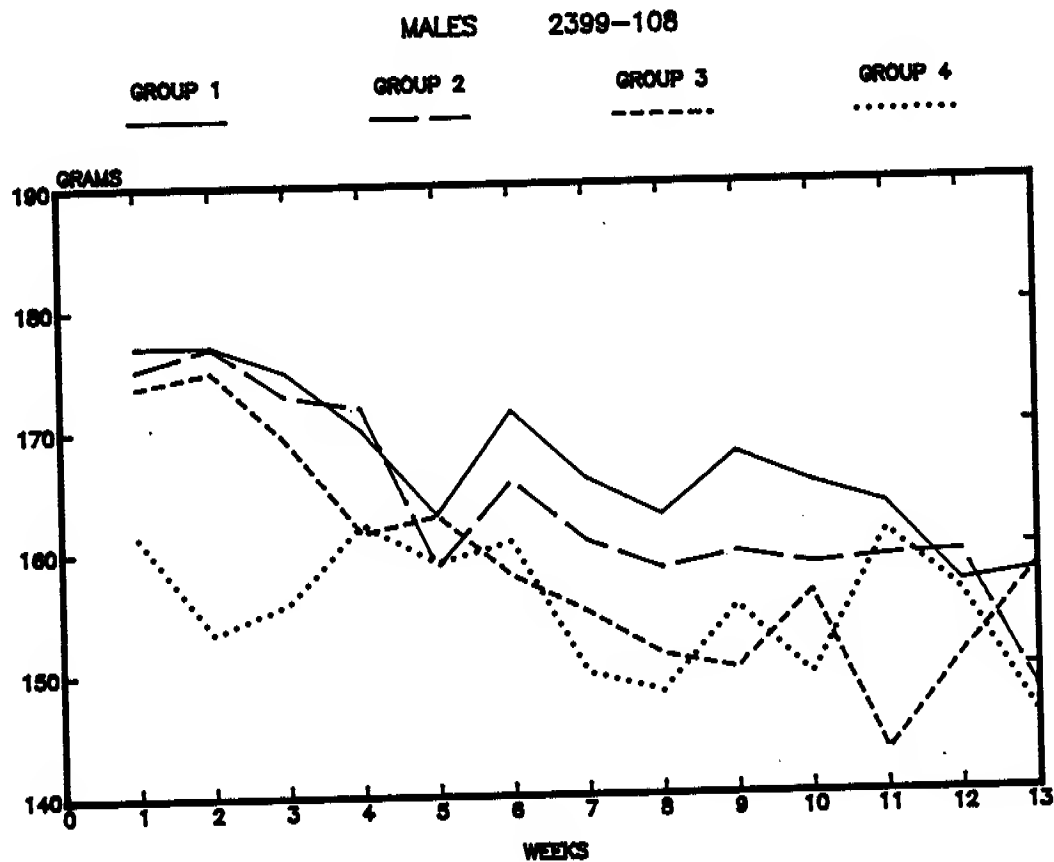
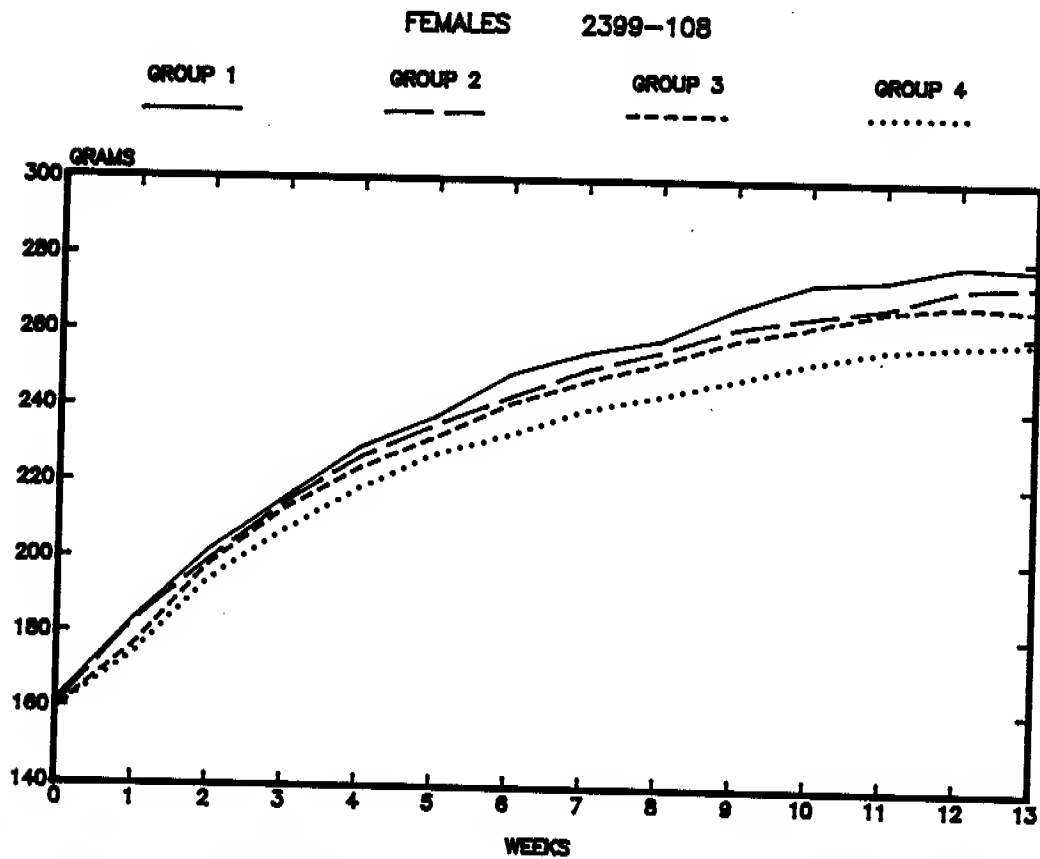
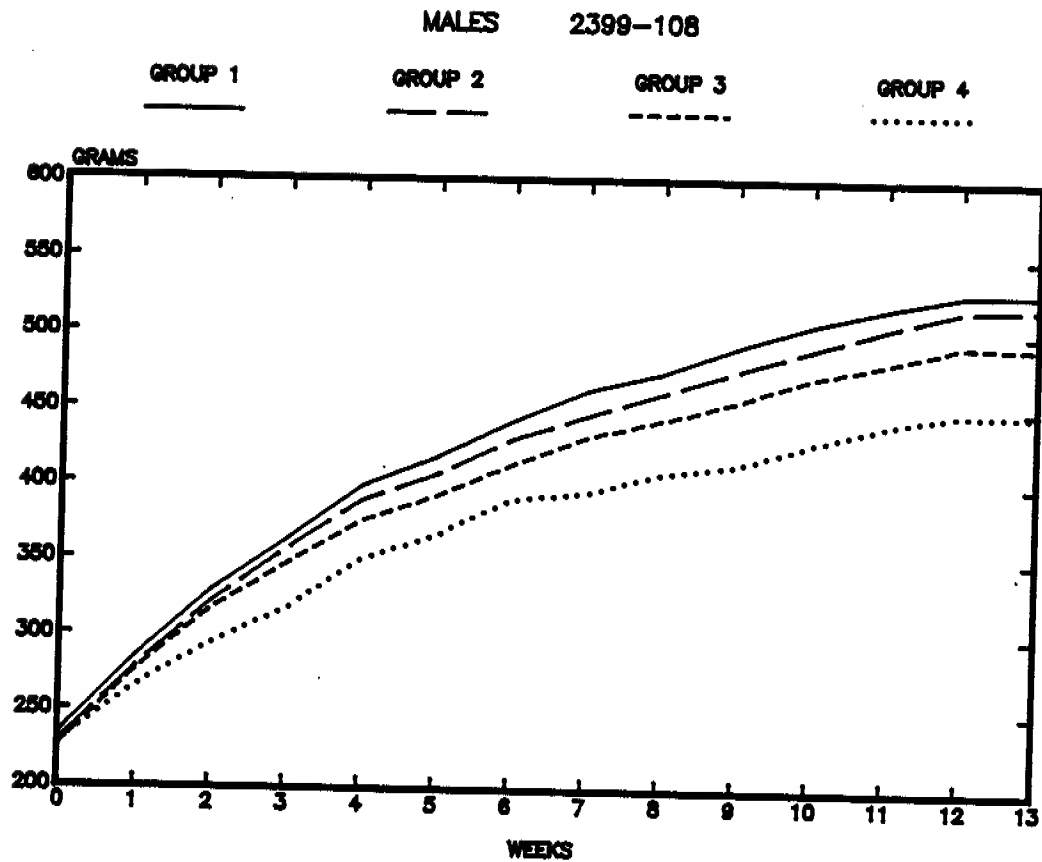


FIGURE 2 - MEAN BODY WEIGHTS

HLA 2399-108



- 21 -

were increased in Group 4 and potassium was increased in Groups 3 and 4. There were fewer significant changes at Week 13: alanine aminotransferase was increased in Group 4 males, and calcium and cholesterol were increased in Group 4 females.

Organ Weights and Organ-to-Body Weight Ratios

Mean organ weights (absolute) and organ-to-body weight ratios (relative) are presented in Tables 8 and 9, respectively; individual values are presented in Appendix 8.

The terminal body weight in Group 4 of both sexes was significantly decreased. In the males, there were a few significant changes in organ weights, all in Group 4: heart weight was decreased and relative brain and relative kidney weights were increased. In the females, there were no significant changes in absolute or relative organ weights.

Gross Pathology

Gross pathology incidence summaries are presented in Tables 10A (Terminal Sacrifice) and 10B (Unscheduled Deaths); individual gross observations are presented in Appendix 8.

There were few gross lesions observed in this study. The most commonly seen were mottled lungs and failure of the lungs to collapse. Both were observed most frequently in Groups 3 and 4 of both sexes. The other lesions observed were sporadic and showed no apparent dose relationship.

Histopathology

Histopathology incidence summaries are presented in Tables 11A (Terminal Sacrifice) and 11B (Unscheduled Deaths); individual data are presented in Appendix 8. Evaluation of microscopic findings is included in the Pathology Summary.



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- 22 -

In the animals examined at the terminal sacrifice, a variety of spontaneously occurring incidental lesions were observed, none being related to treatment. In the 19 unscheduled deaths, all but one of the animals had foreign material in the alveoli. These deaths were judged to be related to gavage dosing accidents and not to the test material.

Analytical Chemistry

Analytical chemistry methods and results are included as Appendix 9.

Stability data showed there was little loss of test material after 21 days of storage at room temperature or 5°C refrigeration. Dose verification analyses showed that all samples analyzed were within the specified limits ($\pm 10\%$ of target concentration).

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- 23 -

DISCUSSION

Xylene (mixed) is a mixture of m-Xylene, p-Xylene, o-Xylene, and ethylbenzene. The exact proportion is variable and depends on the material (petroleum or coal tar) from which it is produced. In this study the m-xylene (99% purity) was tested. In previous studies with xylene (mixed) conducted by the NTP in rats, deaths were noted at 4,000 and 6,000 mg/kg in a single dose study and at 2,000 mg/kg in a 14-day study. In the 13-week study all rats at dose levels up to 1,000 mg/kg survived to termination. Also, mean body weights were 15% and 8% lower than control in the males and females, respectively, no signs of clinical toxicity were observed, and no compound-related gross or microscopic lesions were observed. In a 2-year study, males dosed at 1,000 mg/kg has a slightly higher mortality rate than did the vehicle controls, but the number of gavage deaths was also higher. It was postulated that the dosed males resisted gavaging because of the xylenes. In the 2-year study, no nonneoplastic or neoplastic lesions resulted from exposure to xylene (mixed).

In this 90-day study conducted with the m-Xylene isomer, mortality was significantly increased in Group 3 males and Groups 3 and 4 females, the incidence of salivation was increased in Group 4 males and females, body weight gain was decreased in Groups 3 and 4 males and Group 4 females, food consumption was decreased in Group 4, and several changes were noted in clinical pathology and organ weight data. Histopathology revealed no compound-related changes. The deaths in the treated groups are most likely the result of vehicle/test material aspiration since there was no physical evidence of trauma (perforated trachea and/or esophagus) and the low vapor pressure of xylene (about 10 mm Hg at 28°C). Although the findings in this study suggest m-xylene is slightly more toxic than xylene (mixed), these findings are generally consistent with those noted by the NTP using xylene (mixed).



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- 24 -

Based on the results of this study, with the assumption of vehicle and/or test material aspiration producing the deaths in the treated animals, the no-observed-effect-level (NOEL) of m-xylene was 100 mg/kg/day in the males and 200 mg/kg/day in the females.

Study Director

Gary W. Wolfe 5/27/88
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- 25 -

PATHOLOGY SUMMARY

Subchronic Toxicity Study in Rats with m-Xylene

General Protocol

Eighty male and 80 female Sprague-Dawley/Charles River rats were randomly divided into groups of 20 males and 20 females each. Groups were assigned to study according to the following schedule:

<u>Group Number</u>	<u>Number of Animals</u>		<u>Dosage Levels</u> <u>mg/kg/day</u>
	<u>Male</u>	<u>Female</u>	
1 (Control)	20	20	0
2 (Low)	20	20	100
3 (Mid)	20	20	200
4 (High)	20	20	800

The test material was administered by oral gavage, 7 days per week for 13 weeks. Treatment was continued until the day before necropsy. At termination, all surviving animals were killed and necropsied. Tissues were preserved in formalin. Complete tissues, as outlined in the protocol, were examined microscopically from all control and high dose animals and also from all animals not surviving to termination. Gross lesions, lung, liver and kidney were examined from all remaining animals. The following is a summary of histologic findings.

Histopathology

Scheduled Deaths

No treatment-related lesions were observed in animals receiving m-Xylene for 13 weeks. A variety of spontaneously occurring incidental lesions were observed and these were of the type and frequency expected in

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- 26 -

this strain and age of rat. The most commonly observed changes included perivascular/peribronchiolar lymphoid infiltrates in the lung, degenerative cardiomyopathy, foci of mononuclear cells and bile duct inflammation in the liver, chronic progressive nephropathy, chronic inflammation of the Harderian gland, and dilation of the uterus. A low dose female was observed to have a mammary adenocarcinoma. This is an uncommon, but not rare, neoplasm and although it is unusual to observe this in an animal of this age, it is considered to be spontaneous and not related to intake of the test material.

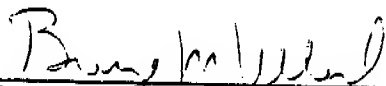
Unscheduled Deaths

Four females and two males from Group 4, five animals of each sex from Group 3 and three males from Group 2 died or were killed moribund on study. The majority of these animals which died on study had foreign material in alveoli. Usually this material elicited little or no inflammatory response although one high dose male developed foreign body pneumonia. This material was transparent and globular but nonrefractile and is felt to be compound and/or vehicle. These deaths are considered to be related to gavage accidents.

Conclusion

Administration of m-Xylene for 13 weeks to male and female rats did not result in treatment-related histomorphologic alterations. Experimental deaths are considered to be related to gavage accidents.

Pathologist:

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- 27 -

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- 28 -

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- 29 -

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- 30 -

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Albumin/Globulin Ratio (A/G RATIO)

Albumin ÷ Globulin = A/G Ratio (Calculated).

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- 31 -

Globulin (GLOBULIN)

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TABLE 1
ADJUSTED SURVIVAL

GROUP	WEEK													
	0	1	2	3	4	5	6	7	8	9	10	11	12	13
<u>Male</u>														
1	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20
2	20/20	20/20	19/20	18/20	18/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20
3	20/20	19/20	19/20	17/20	17/20	16/20	16/20	16/20	15/20	15/20	15/20	15/20	15/20	15/20
4	20/20	20/20	20/20	19/20	19/20	19/20	19/20	19/20	18/20	18/20	18/20	18/20	18/20	18/20
<u>Female</u>														
1	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20
2	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20
3	20/20	20/20	18/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	16/20
4	20/20	20/20	18/20	18/20	18/20	18/20	18/20	17/20	17/20	17/20	17/20	16/20	16/20	16/20

TABLE 2
SUMMARY INCIDENCE OF CLINICAL SIGNS ^a
2399-108

OBSERVATION	MALES				FEMALES			
	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 1	GROUP 2	GROUP 3	GROUP 4
MALOCCLUSION	2	2	2	0	1	0	0	0
SALIVATION	0	0	0	0	0	0	0	1
URINE STAINS	0	0	0	3	0	0	0	4
ALOPECIA	0	0	0	1	0	0	2	1
SORES	0	1	0	2	2	0	0	0
BLOODY CRUST	1	0	0	2	1	0	0	0
CHROMODACRYORRHEA	3	1	2	2	2	0	0	0
SMALL MOVEABLE TISSUE MASS	0	0	0	1	0	0	0	0

^a Total incidence for entire study.

TABLE 3
INCIDENCE OF DAILY OBSERVATIONS^a
(Weekly Totals by Sex and Group)

Incidence of Convulsions

GROUP	WEEK													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14 ^b
<u>Male</u>														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	1/19	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	1/20	-	-	-	-	-	-	-	-	-	-	-
<u>Female</u>														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	2/20	-	-	-	-	-	-	-	-	-	-	-	-

^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates no incidence during week.

^bPartial week (terminal sacrifice)

TABLE 3
INCIDENCE OF DAILY OBSERVATIONS^a
(Weekly Totals by Sex and Group)

Incidence of Hyperactivity

GROUP	WEEK													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14 ^b
<u>Male</u>														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Female</u>														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	3/19	-	-	-	-	-	-	-	-	-	-	-	-
4	-	2/20	-	-	-	-	-	-	-	-	-	-	-	-

^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates no incidence during week.

^bPartial week (terminal sacrifice)

TABLE 3
INCIDENCE OF DAILY OBSERVATIONS^a
(Weekly Totals by Sex and Group)

Incidence of Epistaxis

GROUP	WEEK													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14 ^b
Male														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	2/20	-	-	-	-	-	-	-	-	-	-	-	-
Female														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	1/20	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	1/20	3/20	-	-	-	-	-	-	-	-	-	-	-	-

^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates no incidence during week.

^bPartial week (terminal sacrifice)

TABLE 3
INCIDENCE OF DAILY OBSERVATIONS^a
(Weekly Totals by Sex and Group)

Incidence of Salivation

GROUP	WEEK													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14 ^b
<u>Male</u>														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	16/20	14/20	11/19	2/19	8/19	7/19	1/19	4/18	2/18	2/18	-	1/18	-
<u>Female</u>														
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	1/20	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	1/18	-	-	-	-	-	-	1/17	-	-	-	-
4	6/20	39/20	46/18	50/18	43/18	48/18	38/18	29/17	25/17	22/17	20/16	25/16	28/16	10/16

^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates no incidence during week.

^bPartial week (terminal sacrifice)

TABLE 4A
MEAN BODY WEIGHTS AND STANDARD DEVIATIONS (G)
SUBCHRONIC TOXICITY IN RATS

GROUP AND DOSE LEVEL (MG/KG)	WEEK: START	1	2	3	4	5	6	7	8	9	10	11	12	13
MALES														
1	MEAN	234.5	284.8	328.6	362.8	398.4	418.1	442.1	462.4	474.2	491.8	506.5	517.8	527.8
	S.D.	6.84	9.72	13.52	18.35	22.92	26.60	28.79	29.51	31.81	34.54	36.57	41.09	45.57
	N	20	20	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	229.2	277.8	321.1	356.5	388.8	406.5	430.0	445.9	461.8	476.1	490.4	504.7	518.1
	S.D.	9.04	15.15	21.28	22.24	24.91	24.17	26.70	32.01	32.69	35.44	35.26	38.46	37.79
	N	20	20	19	18	18	17	17	17	17	17	17	17	17
100.000														
3	MEAN	226.9	275.8	316.5	346.8	375.5	392.1	413.2	431.8	443.1	456.1	471.5	481.7	493.2
	S.D.	10.40	9.55	13.24	16.02	19.19	25.01	25.13	24.73	25.72	24.40	24.24	23.26	25.57
	N	20	19	17	17	17	16	16	16	15	15	15	15	15
200.000														
4	MEAN	228.8	265.1	293.4	317.0	349.8	366.5	390.2	394.8	407.7	413.6	428.1	441.0	448.1
	S.D.	8.85	17.74	24.28	24.76	20.98	24.71	23.73	26.07	26.32	27.98	25.85	27.34	33.47
	N	20	20	19	19	19	19	19	19	18	18	18	18	18
800.000														
FEMALES														
1	MEAN	162.0	183.4	201.8	215.7	229.3	237.5	249.1	254.9	258.4	267.0	273.5	274.8	277.9
	S.D.	5.34	7.79	8.99	11.59	14.16	15.89	19.02	20.25	21.41	19.46	22.49	20.34	19.81
	N	20	20	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	160.4	182.7	199.2	214.4	226.7	235.4	243.1	250.4	255.4	261.7	264.9	267.5	273.7
	S.D.	6.31	6.51	8.25	10.14	10.33	11.43	11.36	13.17	11.69	12.29	12.35	14.08	15.32
	N	20	20	20	20	20	20	20	20	20	20	20	20	20
100.000														
3	MEAN	159.7	176.4	198.0	212.9	223.9	232.2	241.2	247.4	252.3	258.7	262.2	266.6	267.2
	S.D.	5.82	6.86	9.64	10.57	15.28	12.80	12.25	16.04	13.72	13.42	14.84	16.59	17.08
	N	20	20	18	17	17	17	17	17	17	17	17	17	16
200.000														
4	MEAN	159.6	174.0	193.9	207.2	218.4	227.7	233.0	239.7	243.6	248.1	252.6	256.3	257.8
	S.D.	7.75	9.33	12.10	14.57	13.04	14.71	16.41	15.13	15.28	13.96	14.51	13.56	15.89
	N	20	20	18	18	18	18	18	17	17	17	17	16	16
800.000														

TABLE 4B
 MEAN BODY WEIGHT CHANGE (G)
 SUBCHRONIC TOXICITY IN RATS
 HLA 2399103

GROUP AND DOSE LEVEL (MG/KG)	0 - 13			WEEK		

	MALES					
1	MEAN	293.3				
	S.D.	43.46				
.000	N	20				
2	MEAN	289.5				
	S.D.	30.61				
100.000	N	17				
3	MEAN	265.2 ^S				
	S.D.	30.37				
200.000	N	15				
4	MEAN	219.5 ^S				
	S.D.	26.16				
800.000	N	18				
	FEMALES					
1	MEAN	115.9				
	S.D.	18.00				
.000	N	20				
2	MEAN	113.2				
	S.D.	14.06				
100.000	N	20				
3	MEAN	107.2				
	S.D.	14.86				
200.000	N	16				
4	MEAN	98.1 ^S				
	S.D.	16.21				
800.000	N	16				

HLA 2399108

TABLE 5A
MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS (G/WK)
SUBCHRONIC TOXICITY IN RATS

GROUP AND DOSE LEVEL (MG/KG)	WEEK: 1	2	3	4	5	6	7	8	9	10	11	12	13
	MALES												
1	MEAN 177.0	177.0	174.8	170.0	162.9	171.4	165.8	162.8	167.8	165.3	163.5	156.9	157.8
	S.D. 14.88	10.53	12.96	18.21	15.74	13.87	13.19	12.96	13.88	13.89	15.94	17.93	13.89
	N 20	20	20	20	10	20	20	20	20	20	19	20	10
2	MEAN 175.1	176.9	172.8	171.8	158.6	165.7	160.6	158.3	159.6	158.6	159.1	159.4	148.2
	S.D. 14.89	14.71	10.27	14.18	8.52	13.54	15.84	10.99	12.04	9.66	11.00	9.44	12.11
	N 20	18	17	18	7	17	16	16	16	17	16	17	7
100.000	MEAN 173.6	174.9	169.1	161.5	162.8	157.8	154.8	151.2	150.0	156.3	143.1	150.9	158.1
	S.D. 10.86	11.03	10.40	15.22	4.05	10.25	7.30	10.28	9.84	9.80	18.26	14.41	17.92
	N 19	19	17	17	6	16	15	15	15	15	11	15	5
200.000	MEAN 161.3	153.3	155.7	162.2	159.0	160.7	149.8	148.2	155.2	149.4	161.2	156.2	146.0
	S.D. 17.89	23.78	19.20	16.37	16.39	13.89	15.20	19.03	17.29	11.85	20.29	21.78	17.78
	N 20	20	19	18	9	19	16	15	18	14	18	18	8
	FEMALES												
1	MEAN 130.3	133.5	133.1	123.4	120.1	131.4	126.5	120.7	126.3	127.6	116.2	115.7	114.5
	S.D. 10.52	13.03	10.13	13.77	13.65	14.71	13.20	16.31	18.23	12.45	9.30	10.38	9.86
	N 20	20	17	18	10	19	19	15	19	18	15	20	10
2	MEAN 138.1	132.7	139.2	126.1	125.1	130.0	123.6	129.5	125.6	122.3	119.2	118.2	126.1
	S.D. 14.39	11.28	11.74	11.58	14.13	14.43	11.42	22.02	15.19	9.90	11.11	14.96	31.06
	N 19	19	17	20	10	19	19	19	19	20	18	19	9
100.000	MEAN 134.2	136.8	139.3	125.6	122.3	127.5	121.6	122.8	126.7	121.3	114.1	120.5	116.0
	S.D. 15.39	14.67	13.03	13.79	12.47	13.61	11.29	18.59	17.78	11.65	12.25	19.88	11.83
	N 19	18	15	16	7	16	15	17	16	15	16	17	6
200.000	MEAN 127.8	132.3	135.3	132.2	138.0	126.0	119.6	122.9	126.9	120.0	129.8	123.1	126.6
	S.D. 10.58	17.92	12.00	12.20	19.55	24.63	8.35	14.76	15.56	14.15	24.37	18.17	19.65
	N 20	18	15	13	7	17	12	14	15	14	14	16	6

TABLE 5B
MEAN TOTAL FOOD CONSUMPTION AND STANDARD DEVIATIONS (G)
SUBCHRONIC TOXICITY IN RATS

GROUP AND DOSE LEVEL (MG/KG)	WEEK			
	1 - 5	6 - 9	10 - 13	
MALES				
1	MEAN	860.0	667.8	644.3
.000	S.D.	66.03	48.31	52.29
	N	10	20	9
2	MEAN	831.4	640.6	611.6
100.000	S.D.	46.07	42.88	39.33
	N	6	14	6
3	MEAN	849.5	611.7 ^S	614.6
200.000	S.D.	25.81	30.73	23.15
	N	6	14	4
4	MEAN	773.6 ^S	612.0 ^S	586.8
800.000	S.D.	59.64	55.08	28.92
	N	8	14	5
FEMALES				
1	MEAN	634.9	511.4	472.4
.000	S.D.	56.91	46.89	28.32
	N	8	13	9
2	MEAN	650.1	505.4	478.0
100.000	S.D.	56.50	48.52	52.80
	N	9	17	8
3	MEAN	678.9	493.4	465.6
200.000	S.D.	38.24	50.78	40.62
	N	5	15	6
4	MEAN	656.8	479.7	488.8
800.000	S.D.	46.35	33.23	43.20
	N	5	10	6

Table 6
HEAR CLINICAL PHOTODUPLICATION
SUBJECTIVE TOXICITY STUDY IN RATS

GROUP AND DOSAGE LEVEL	RE	MT/01		MT/02		MT/03		MT/04		MT/05		MT/06		MT/07		MT/08		MT/09		MT/10		MT/11		MT/12		MT/13		MT/14		MT/15		MT/16		MT/17		MT/18		MT/19		MT/20		MT/21		MT/22		MT/23		MT/24		MT/25		MT/26		MT/27		MT/28		MT/29		MT/30		MT/31		MT/32		MT/33		MT/34		MT/35		MT/36		MT/37		MT/38		MT/39		MT/40		MT/41		MT/42		MT/43		MT/44		MT/45		MT/46		MT/47		MT/48		MT/49		MT/50		MT/51		MT/52		MT/53		MT/54		MT/55		MT/56		MT/57		MT/58		MT/59		MT/60		MT/61		MT/62		MT/63		MT/64		MT/65		MT/66		MT/67		MT/68		MT/69		MT/70		MT/71		MT/72		MT/73		MT/74		MT/75		MT/76		MT/77		MT/78		MT/79		MT/80		MT/81		MT/82		MT/83		MT/84		MT/85		MT/86		MT/87		MT/88		MT/89		MT/90		MT/91		MT/92		MT/93		MT/94		MT/95		MT/96		MT/97		MT/98		MT/99		MT/100		MT/101		MT/102		MT/103		MT/104		MT/105		MT/106		MT/107		MT/108		MT/109		MT/110		MT/111		MT/112		MT/113		MT/114		MT/115		MT/116		MT/117		MT/118		MT/119		MT/120		MT/121		MT/122		MT/123		MT/124		MT/125		MT/126		MT/127		MT/128		MT/129		MT/130		MT/131		MT/132		MT/133		MT/134		MT/135		MT/136		MT/137		MT/138		MT/139		MT/140		MT/141		MT/142		MT/143		MT/144		MT/145		MT/146		MT/147		MT/148		MT/149		MT/150		MT/151		MT/152		MT/153		MT/154		MT/155		MT/156		MT/157		MT/158		MT/159		MT/160		MT/161		MT/162		MT/163		MT/164		MT/165		MT/166		MT/167		MT/168		MT/169		MT/170		MT/171		MT/172		MT/173		MT/174		MT/175		MT/176		MT/177		MT/178		MT/179		MT/180		MT/181		MT/182		MT/183		MT/184		MT/185		MT/186		MT/187		MT/188		MT/189		MT/190		MT/191		MT/192		MT/193		MT/194		MT/195		MT/196		MT/197		MT/198		MT/199		MT/200		MT/201		MT/202		MT/203		MT/204		MT/205		MT/206		MT/207		MT/208		MT/209		MT/210		MT/211		MT/212		MT/213		MT/214		MT/215		MT/216		MT/217		MT/218		MT/219		MT/220		MT/221		MT/222		MT/223		MT/224		MT/225		MT/226		MT/227		MT/228		MT/229		MT/230		MT/231		MT/232		MT/233		MT/234		MT/235		MT/236		MT/237		MT/238		MT/239		MT/240		MT/241		MT/242		MT/243		MT/244		MT/245		MT/246		MT/247		MT/248		MT/249		MT/250		MT/251		MT/252		MT/253		MT/254		MT/255		MT/256		MT/257		MT/258		MT/259		MT/260		MT/261		MT/262		MT/263		MT/264		MT/265		MT/266		MT/267		MT/268		MT/269		MT/270		MT/271		MT/272		MT/273		MT/274		MT/275		MT/276		MT/277		MT/278		MT/279		MT/280		MT/281		MT/282		MT/283		MT/284		MT/285		MT/286		MT/287		MT/288		MT/289		MT/290		MT/291		MT/292		MT/293		MT/294		MT/295		MT/296		MT/297		MT/298		MT/299		MT/300		MT/301		MT/302		MT/303		MT/304		MT/305		MT/306		MT/307		MT/308		MT/309		MT/310		MT/311		MT/312		MT/313		MT/314		MT/315		MT/316		MT/317		MT/318		MT/319		MT/320		MT/321		MT/322		MT/323		MT/324		MT/325		MT/326		MT/327		MT/328		MT/329		MT/330		MT/331		MT/332		MT/333		MT/334		MT/335		MT/336		MT/337		MT/338		MT/339		MT/340		MT/341		MT/342		MT/343		MT/344		MT/345		MT/346		MT/347		MT/348		MT/349		MT/350		MT/351		MT/352		MT/353		MT/354		MT/355		MT/356		MT/357		MT/358		MT/359		MT/360		MT/361		MT/362		MT/363		MT/364		MT/365		MT/366		MT/367		MT/368		MT/369		MT/370		MT/371		MT/372		MT/373		MT/374		MT/375		MT/376		MT/377		MT/378		MT/379		MT/380		MT/381		MT/382		MT/383		MT/384		MT/385		MT/386		MT/387		MT/388		MT/389		MT/390		MT/391		MT/392		MT/393		MT/394		MT/395		MT/396		MT/397		MT/398		MT/399		MT/400		MT/401		MT/402		MT/403		MT/404		MT/405		MT/406		MT/407		MT/408		MT/409		MT/410		MT/411		MT/412		MT/413		MT/414		MT/415		MT/416		MT/417		MT/418		MT/419		MT/420		MT/421		MT/422		MT/423		MT/424		MT/425		MT/426		MT/427		MT/428		MT/429		MT/430		MT/431		MT/432		MT/433		MT/434		MT/435		MT/436		MT/437		MT/438		MT/439		MT/4
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TABLE 6 - CONTINUED
 MEAN CLINICAL REPRODUCTION VALUES
 SUBSEQUENT FERTILITY STUDY IN RATS

GROUP AND DOSE LEVEL	DIFF			BRAY			DIFF			DIFF			DIFF			DIFF		
	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N
1 0 MG/KG	16.3	3.48	10	16.3	3.36	10	16.3	3.21	10	16.3	3.49	10	16.3	3.34	10	16.3	3.41	10
2 100 MG/KG	15.3	3.49	10	14.5	3.21	10	15.3	3.49	10	14.5	3.21	10	15.3	3.49	10	14.5	3.21	10
3 200 MG/KG	18.4	5.34	10	17.3	4.02	10	18.4	5.34	10	17.3	4.02	10	18.4	5.34	10	17.3	4.02	10
4 800 MG/KG	17.3	4.41	10	16.6	4.56	10	17.3	4.41	10	16.6	4.56	10	17.3	4.41	10	16.6	4.56	10
5 BASELINE	13.2	3.01	5															
1 0 MG/KG	14.0	3.60	10	11.8	1.76	10	14.0	3.60	10	11.8	1.76	10	14.0	3.60	10	11.8	1.76	10
2 100 MG/KG	13.8	3.72	10	12.6	2.63	10	13.8	3.72	10	12.6	2.63	10	13.8	3.72	10	12.6	2.63	10
3 200 MG/KG	14.3	3.40	10	12.3	3.53	10	14.3	3.40	10	12.3	3.53	10	14.3	3.40	10	12.3	3.53	10
4 800 MG/KG	14.9	2.86	10	13.7	3.32	10	14.9	2.86	10	13.7	3.32	10	14.9	2.86	10	13.7	3.32	10
5 BASELINE	15.4	2.50	5															

TABLE 6 - CONTINUED
MEAN CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS

GROUP AND DOSAGE LEVEL	S.G. TH/UL (%)			LYMPH TH/UL (%)			RBC TH/UL (%)			EOSIN TH/UL (%)		
	5	13	-1	5	13	-1	5	13	-1	5	13	-1
MALE												
1 0 MG/KG	MEAN S.D. N	2.6 1.91 10	2.5 1.10 10	13.5 3.74 10	13.6 2.92 10		.1 .13 10	.1 .13 10		.1 .11 10	.1 .09 10	
2 100 MG/KG	MEAN S.D. N	1.9 .88 10	2.4 2.23 10	13.8 3.45 10	12.0 2.75 10		.1 .11 10	.0 .07 10		.2 .20 10	.1 .15 10	
3 200 MG/KG	MEAN S.D. N	2.6 1.42 10	2.7 1.82 10	15.4 5.16 10	14.2 2.70 10		.2 .20 10	.1 .11 10		.2 .19 10	.2 .15 10	
4 800 MG/KG	MEAN S.D. N	2.5 1.55 10	2.4 1.48 10	14.3 3.66 10	14.0 4.21 10		.2 .19 10	.1 .10 10		.3 .22 10	.2 .16 10	
5 BASELINE	MEAN S.D. N	.8 .37 5		11.9 2.94 5		.4 .24 5			.1 .08 5			
FEMALE												
1 0 MG/KG	MEAN S.D. N	2.2 .84 10	1.8 .76 10	11.5 3.45 10	9.8 1.84 10		.1 .11 10	.1 .10 10		.1 .13 10	.1 .13 10	
2 100 MG/KG	MEAN S.D. N	1.9 1.02 10	2.1 1.03 10	11.5 3.37 10	10.2 2.21 10		.1 .17 10	.1 .13 10		.2 .21 10	.3 .28 10	
3 200 MG/KG	MEAN S.D. N	1.8 .68 10	1.6 1.06 10	12.2 3.41 10	10.5 2.28 10		.1 .14 10	.0 .07 10		.2 .21 10	.1 .14 10	
4 800 MG/KG	MEAN S.D. N	1.5 .75 10	2.7 1.71 10	13.0 2.81 10	10.7 3.30 10		.2 .21 10	.1 .16 10		.2 .18 10	.2 .10 10	
5 BASELINE	MEAN S.D. N	1.1 .48 5		13.8 2.48 5		.3 .22 5			.2 .19 5			

TABLE 6 - CONTINUED
MEAN CLINICAL HEMATOLOGY VALUES
SUBHEPATIC TOXICITY STUDY IN RATS

GROUP AND DOSAGE LEVEL	BASED TH. H. (%)			
	DIFF			
	-1	5	13	
1 0 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
2 100 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
3 200 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
4 800 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
5 BASELINE	MEAN S.D. N	.0 .00 5		
1 0 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
2 100 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
3 200 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
4 800 MG/KG	MEAN S.D. N	.0 .00 10	.0 .00 10	.0 .00 10
5 BASELINE	MEAN S.D. N	.0 .00 5		

F+Male

TABLE 2
DEATH CLINICAL TRIALS BY GROUPS
SUBCUTANEOUS INJECTIONS IN RATS

GROUP AND DOSAGE LEVEL	SUDAN			POLAR			EVALUATE			T POOL		
	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N
1 0 MG/KG	148.0	1.56	10	146.1	1.91	10	6.01	6.25	10	104.5	104.3	10
2 100 MG/KG	146.7	1.34	10	146.0	1.96	10	6.31	6.30	10	104.6	103.7	10
3 200 MG/KG	147.3	1.50	10	145.5	1.65	10	6.37	6.18	10	104.0	104.3	10
4 800 MG/KG	147.6	1.34	10	146.0	1.60	10	6.56	6.58	10	105.0	104.7	10
5 BASELINE	145.9	2.13	5	145.9	2.13	5	6.61	6.61	5	103.4	103.4	5
1 0 MG/KG	145.3	1.28	10	144.5	1.29	10	5.71	6.16	10	106.0	106.0	10
2 100 MG/KG	144.8	1.95	10	145.0	1.34	10	5.99	6.14	10	106.4	106.8	10
3 200 MG/KG	145.2	1.91	10	144.4	1.23	10	6.13	5.98	10	107.2	106.3	10
4 800 MG/KG	145.4	1.56	10	144.6	1.41	10	6.16	6.22	10	105.3	106.2	10
5 BASELINE	145.5	1.57	5	145.5	1.57	5	6.52	6.52	5	106.7	106.7	5

TABLE 2 - CONTINUED
HEART CLINICAL TRIALISTRY RESULTS
SUBCUTANEOUS INJECTORY STUDY IN RATS

GROUP AND DOSE LEVEL	ALBUMIN (G/DL)			CALCULATED (G/DL)			G.U. (G/DL)			CALCULATED (G/DL)			G.U. (G/DL)		
	-1	5	13	-1	5	13	-1	5	13	-1	5	13	-1	5	13
1 0 MG/KG	MEAN S.D. N	3.8 .23 10	3.7 .15 10	2.1 .18 10	2.6 .33 10	2.6 .15 10	1.80 .128 10	1.43 .120 10	10.0 .33 10	9.6 .66 10					
2 100 MG/KG	MEAN S.D. N	3.9 .21 10	3.8 .19 10	2.1 .26 10	2.6 .15 10	2.6 .15 10	1.90 .302 10	1.45 .133 10	10.1 .41 10	9.8 .41 10					
3 200 MG/KG	MEAN S.D. N	3.8 .14 10	3.7 .13 10	2.1 .19 10	2.6 .14 10	2.6 .14 10	1.81 .200 10	1.44 .112 10	10.1 .34 10	9.7 .59 10					
4 800 MG/KG	MEAN S.D. N	3.8 .20 10	3.8 .35 10	2.1 .23 10	2.4 .23 10	2.4 .23 10	1.86 .266 10	1.56 .230 10	10.1 .23 10	9.7 .59 10					
5 BASELINE	MEAN S.D. N	3.8 .31 5		1.9 .15 5			2.01 .162 5		10.4 .43 5						
1 0 MG/KG	MEAN S.D. N	4.1 .37 10	4.1 .26 10	2.0 .24 10	2.6 .20 10	2.6 .20 10	2.06 .394 10	1.59 .122 10	9.9 .36 10	9.8 .30 10					
2 100 MG/KG	MEAN S.D. N	4.1 .30 10	4.1 .20 10	2.1 .25 10	2.5 .26 10	2.5 .26 10	1.97 .324 10	1.64 .131 10	9.9 .39 10	10.0 .39 10					
3 200 MG/KG	MEAN S.D. N	4.1 .28 10	4.1 .31 10	2.1 .20 10	2.6 .14 10	2.6 .14 10	1.94 .262 10	1.55 .166 10	10.2 .33 10	10.0 .33 10					
4 800 MG/KG	MEAN S.D. N	4.0 .18 10	4.1 .31 10	2.1 .26 10	2.7 .24 10	2.7 .24 10	1.92 .264 10	1.54 .211 10	10.4 ^s .33 10	10.2 ^s .18 10					
5 BASELINE	MEAN S.D. N	4.0 .19 5		1.8 .11 5			2.19 .11 5		10.7 .60 5						

TABLE 7 - CONTINUED
MEAN CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS

GROUP AND DOSAGE LEVEL	AST			ALT			U/L			ALK P			U/L			LOH		
	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N
1	81	18.6	9	27	5.8	9	24	3.7	10	140	44.1	10	74	28.2	10	365	192.5	9
2	77	7.6	10	24	2.9	10	21	4.1	10	117	17.0	10	80	14.4	10	466	214.4	10
3	74	9.7	10	26	4.9	10	26	9.5	10	136	35.7	10	69	15.7	10	352	192.4	10
4	79	20.4	10	28	5.5	10	33	8.8	10	105	10.2	10	89	23.7	10	374	209.1	10
5	96	56.7	5	28	7.8	5	201	56.7	5	372	255.5	5	220	138.4	10	215	123.0	10
BASELINE	96	56.7	5	28	7.8	5	201	56.7	5	372	255.5	5	220	138.4	10	215	123.0	10
MALE																		
1	79	16.3	10	25	3.9	10	22	5.5	10	101	26.3	10	47	8.8	10	402	187.3	10
2	82	13.6	10	28	7.3	10	25	6.1	10	100	44.8	10	58	21.1	10	382	119.2	10
3	77	10.1	10	24	3.5	10	24	3.8	10	94	15.7	10	54	13.2	10	442	179.3	10
4	73	8.9	10	25	4.3	10	29	9.1	10	82	25.4	10	49	18.8	10	391	209.6	10
5	102	20.2	5	26	3.7	5	165	33.2	5	580	91.3	5	260	136.2	10	223	72.6	10
BASELINE	102	20.2	5	26	3.7	5	165	33.2	5	580	91.3	5	260	136.2	10	223	72.6	10
FEMALE																		
1	79	16.3	10	25	3.9	10	22	5.5	10	101	26.3	10	47	8.8	10	402	187.3	10
2	82	13.6	10	28	7.3	10	25	6.1	10	100	44.8	10	58	21.1	10	382	119.2	10
3	77	10.1	10	24	3.5	10	24	3.8	10	94	15.7	10	54	13.2	10	442	179.3	10
4	73	8.9	10	25	4.3	10	29	9.1	10	82	25.4	10	49	18.8	10	391	209.6	10
5	102	20.2	5	26	3.7	5	165	33.2	5	580	91.3	5	260	136.2	10	223	72.6	10
BASELINE	102	20.2	5	26	3.7	5	165	33.2	5	580	91.3	5	260	136.2	10	223	72.6	10

^a One animal deleted from statistics; see individual data (Appendix 7).

TABLE 1 - CONTINUED
MEAN CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS

GROUP AND DOSAGE LEVEL	BUN			CREAT			GLUCOSE			T. CHOL		
	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N
1 0 MG/KG	13	2.7	10	13	2.8	10	13	2.8	10	13	2.8	10
2 100 MG/KG	13	2.3	10	12	1.6	10	13	2.8	10	13	2.8	10
3 200 MG/KG	13	2.0	10	14	1.7	10	13	2.8	10	13	2.8	10
4 800 MG/KG	14	5.3	10	13	4.2	10	13	2.8	10	13	2.8	10
5 BASELINE	15	4.7	5	15	4.7	5	15	4.7	5	15	4.7	5
1 0 MG/KG	16	2.9	10	14	1.9	10	16	2.9	10	16	2.9	10
2 100 MG/KG	16	3.2	10	14	1.4	10	16	3.2	10	16	3.2	10
3 200 MG/KG	13	4.1	10	13	2.0	10	13	4.1	10	13	4.1	10
4 800 MG/KG	14	2.8	10	14	2.4	10	14	2.8	10	14	2.8	10
5 BASELINE	15	2.2	5	15	2.2	5	15	2.2	5	15	2.2	5

MALE

1 0 MG/KG	13	2.7	10	13	2.8	10	13	2.8	10	13	2.8	10
2 100 MG/KG	13	2.3	10	12	1.6	10	13	2.8	10	13	2.8	10
3 200 MG/KG	13	2.0	10	14	1.7	10	13	2.8	10	13	2.8	10
4 800 MG/KG	14	5.3	10	13	4.2	10	13	2.8	10	13	2.8	10
5 BASELINE	15	4.7	5	15	4.7	5	15	4.7	5	15	4.7	5

FEMALE

1 0 MG/KG	16	2.9	10	14	1.9	10	16	2.9	10	16	2.9	10
2 100 MG/KG	16	3.2	10	14	1.4	10	16	3.2	10	16	3.2	10
3 200 MG/KG	13	4.1	10	13	2.0	10	13	4.1	10	13	4.1	10
4 800 MG/KG	14	2.8	10	14	2.4	10	14	2.8	10	14	2.8	10
5 BASELINE	15	2.2	5	15	2.2	5	15	2.2	5	15	2.2	5

TABLE 2 - CONTINUED
MEAN CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS

GROUP AND DOSE LEVEL	IN PUPS			T B U L			SEX	N
	DIFF	MG/DL		-1	13	-1	5	13
MALE								
1 0 MG/KG	MEAN S.D. N	8.9 1.02 10	8.6 .98 10	.1 F .05 10	.2 .06 10			
2 100 MG/KG	MEAN S.D. N	8.8 .64 10	8.2 1.25 10	.0 .07 10	.2 .06 10			
3 200 MG/KG	MEAN S.D. N	8.9 .82 10	8.1 1.36 10	.0 .05 10	.2 .08 10			
4 800 MG/KG	MEAN S.D. N	9.1 .85 10	9.1 1.25 10	.0 S .05 10	.2 .05 10			
5 BASELINE	MEAN S.D. N	11.8 1.21 5		.1 .08 5				
FEMALE								
1 0 MG/KG	MEAN S.D. N	8.1 1.23 10	7.4 F 1.95 10	.1 .08 10	.2 .06 10			
2 100 MG/KG	MEAN S.D. N	7.9 1.09 10	7.3 .66 10	.0 .07 10	.2 .06 10			
3 200 MG/KG	MEAN S.D. N	8.4 .86 10	7.3 .83 10	.1 .05 10	.2 .08 10			
4 800 MG/KG	MEAN S.D. N	8.5 .68 10	7.8 1.32 10	.1 .07 10	.2 .05 10			
5 BASELINE	MEAN S.D. N	12.0 1.21 5		.1 .08 5				

TABLE 8
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

STUDY NUMBER: 2399108

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

ABSOLUTE ORGAN WEIGHT MEANS (g)

TABLE INCLUDES:
SEX=ALL; GROUP=ALL; WEEKS=ALL
DEATH=T; SUBSET=ALL

SEX:		MALE				FEMALE			
GROUP:		1	2	3	4	1	2	3	4
NUMBER:		20	17	15	18	20	20	15	16
>>> TERMINAL BODY WEIGHT (g) <<<									
# IN GRP.:		20	17	15	18	20	20	15	16
MEAN:		507.2	478.6	472.5	437.0 ^s	263.1	258.4	255.6	243.7 ^s
STAND DEV:		44.9	74.7	30.8	61.5	18.5	14.8	14.6	19.4
>>> AD - ADRENAL <<<									
# IN GRP.:		15	7	5	8	15	10	6	6
MEAN:		.055	.050	.056	.051	.068	.068	.070	.068
STAND DEV:		.007	.004	.013	.007	.013	.009	.012	.008
>>> OV - OVARY <<<									
# IN GRP.:		0	0	0	0	15	10	6	6
MEAN:						.124	.115	.124	.111
STAND DEV:						.029	.019	.013	.011
>>> BR - BRAIN W/STEM <<<									
# IN GRP.:		15	7	5	8	15	10	6	6
MEAN:		2.05	2.09	2.09	2.01	1.97	1.93	1.90	1.97
STAND DEV:		.08	.07	.15	.11	.09	.09	.06	.09
>>> HT - HEART <<<									
# IN GRP.:		15	7	5	8	15	10	6	6
MEAN:		1.36	1.32	1.25	1.12 ^s	.85	.85	.81	.77
STAND DEV:		.13	.06	.09	.11	.10	.05	.06	.08
>>> SP - SPLEEN <<<									
# IN GRP.:		15	7	5	8	15	10	6	6
MEAN:		.84	.76	.79	.67	.54	.54	.55	.53
STAND DEV:		.18	.06	.11	.12	.06	.11	.10	.04

TABLE 8
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88
PAGE: 54

STUDY NUMBER: 2399108

ABSOLUTE ORGAN WEIGHT MEANS (g)

TABLE INCLUDES:

SEX=ALL; GROUP=ALL; WEEKS=ALL
DEATH=T; SUBSET=ALL

SEX:	MALE				FEMALE			
	1	2	3	4	1	2	3	4
GROUP:	20	17	15	18	20	20	15	16
NUMBER:								
# IN GRP.:	15	7	5	8	15	10	6	6
MEAN:	3.22	3.03	3.27	3.21	1.84	1.84	1.87	1.91
STAND DEV:	.31	.29	.30	.19	.16	.20	.17	.13
>>> KD - KIDNEY <<<								
# IN GRP.:	15	7	5	8	15	10	6	6
MEAN:	13.11	12.72	12.79	12.51	7.39	7.78	7.81	7.89
STAND DEV:	1.83	1.20	1.66	1.44	1.49	1.21	1.71	.79
>>> LI - LIVER <<<								
# IN GRP.:	15	7	5	8	15	10	6	6
MEAN:	5.16	5.07	5.15	5.02	0	0	0	0
STAND DEV:	.35	.44	.21	.54				
>>> TP - TESTIS/EPIDID <<<								
# IN GRP.:	15	7	5	8	0	0	0	0
MEAN:	5.16	5.07	5.15	5.02				
STAND DEV:	.35	.44	.21	.54				

TABLE INCLUDES:

SEX=ALL; GROUP=ALL; WEEKS=ALL
DEATH=T; SUBSET=ALL

SEX:		MALE			FEMALE		
GROUP:	NUMBER:	1	2	3	1	2	3
GROUP:	NUMBER:	20	17	15	20	20	15
>>> AD - ADRENAL <<<		>>> QU - QUARY <<<			>>> HT - HEART <<<		
# IN GRP.:	15	7	5	15	10	6	6
MEAN:	.0110	.0119	.0114	.0120	.0258	.0264	.0286
STAND DEV:	.0019	.0046	.0022	.0020	.0050	.0045	.0047
# IN GRP.:	0	0	0	15	0	10	6
MEAN:				.0477	.0444	.0505	.0458
STAND DEV:				.0123	.0056	.0038	.0054
>>> BR - BRAIN W/STEM <<<		>>> SP - SPLEEN <<<			>>> KD - KIDNEY <<<		
# IN GRP.:	15	7	5	15	10	6	6
MEAN:	.404	.496	.427	.469	.754	.750	.815
STAND DEV:	.039	.184	.036	.038	.063	.064	.073
# IN GRP.:	15	7	5	15	10	6	6
MEAN:	.266	.312	.256	.262	.323	.327	.318
STAND DEV:	.021	.112	.024	.031	.044	.023	.017
# IN GRP.:	15	7	5	15	10	6	6
MEAN:	.164	.180	.161	.157	.204	.207	.219
STAND DEV:	.034	.067	.027	.027	.027	.041	.011
# IN GRP.:	15	7	5	15	10	6	6
MEAN:	.630	.732	.666	.749	.703	.713	.788
STAND DEV:	.047	.339	.024	.046	.073	.088	.055

TABLE 9
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

ORGAN TO TERMINAL BODY WEIGHT RATIO MEANS (%)

STUDY NUMBER: 2399108

TABLE INCLUDES:

SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX:		MALE				FEMALE			
GROUP:	NUMBER:	1	2	3	4	1	2	3	4
		20	17	15	18	20	20	15	16
>>> LI - LIVER <<<									
# IN GRP.:	15	5	7	5	8	15	10	6	6
MEAN:	2.562	2.604	3.037	2.908	2.819	3.022	3.195	3.266	3.373
STAND DEV:	.312	.239	1.266	.253	.569	.546	.712	.373	.373
>>> TP - TESTIS/EPIDID <<<									
# IN GRP.:	15	5	7	5	8	0	0	0	0
MEAN:	1.014	1.055	1.203	1.171					
STAND DEV:	.083	.085	.447	.125					

TABLE 10A
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
GROSS PATHOLOGY INCIDENCE SUMMARY

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---

TABLE INCLUDES: SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH=T;SUBSET=ALL									
ORGAN AND KEYWORD(S) OR PHRASE	SEX:		-----MALE-----				-----FEMALE-----		
	GROUP:	-1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-
	NUMBER:	20	17	15	18	20	20	15	16
** TOP OF LIST **									
BRAIN W/STEM (BR)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16
	NOT REMARKABLE:	20	17	15	18	20	20	15	16
PITUITARY (PI)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16
	NOT REMARKABLE:	20	17	15	18	20	20	15	16
CORD, CERVICAL (CS)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16
	NOT REMARKABLE:	20	17	15	18	20	20	15	16
CORD, THORACIC (TC)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16
	NOT REMARKABLE:	20	17	15	18	20	20	15	16
CORD, LUMBAR (LC)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16
	NOT REMARKABLE:	20	17	15	18	20	20	15	16
NERVE, SCIATIC (SN)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16
	NOT REMARKABLE:	20	17	15	18	20	20	15	16
LUNG (LU)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16
	NOT REMARKABLE:	20	17	15	17	20	20	15	16
DARK AREA		0	0	0	1	0	0	0	0

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLUDES:
SEX=ALL; GROUP=ALL; WEEKS=ALL
DEATH=T; SUBSET=ALL

--- NUMBER - OF - ANIMALS - AFFECTED ---

SEX: ---MALE--- ---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 20 17 15 18 20 20 20 15 16

ORGAN AND KEYWORD(S) OR PHRASE

KIDNEY (KD) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 19 17 14 16 18 18 15 15 16

PELVIS, DILATED
PELVIS, FLUID
PELVIS, GRANULAR MATERIAL
PALE AREA
H-PELVIS, DILATED
1 0 1 2 0 2 0 0 0
0 0 0 1 0 0 0 0 0
0 0 0 1 0 0 0 0 0
1 0 0 0 1 0 0 0 0

ADRENAL, MEDULLA (AM) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

ADRENAL, CORTEX (AC) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

LIVER (LI) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 17 20 20 20 15 16

RAISED AREA
0 0 0 1 0 0 0 0 0

SPLEEN (SP) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

PANCREAS (PA) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

HEART (HT) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

TABLE 10A

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88
PAGE: 59

STUDY NUMBER: 2399108

GROSS PATHOLOGY INCIDENCE SUMMARY

--- NUMBER - OF - ANIMALS - AFFECTED ---

TABLE INCLUDES:

SEX=ALL; GROUP=ALL; WEEKS=ALL
DEATH=T; SUBSET=ALL

SEX:

-----MALE-----

-----FEMALE-----

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

ORGAN AND KEYWORD(S) OR PHRASE

NUMBER: 20 17 15 18 20 20 15 16

THYMUS (TH)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 15 16

TRACHEA (TR)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 15 16

THYROID (TY)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 15 16

PARATHYROID (PT)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 15 16

ESOPHAGUS (ES)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 15 16

MAND SALIVARY GL (SG)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 15 16

AORTA, THORACIC (AO)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 15 16

STOMACH, GL (ST)

NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 14 16

DARK AREA

0 0 0 0 0 0 0 1 0

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---												
TABLE INCLUDES:		SEX:		-----MALE-----				-----FEMALE-----				
SEX=ALL; GROUP=ALL; WEEKS=ALL DEATH=T; SUBSET=ALL		GROUP:		-1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-	
ORGAN AND KEYWORD(S) OR PHRASE		NUMBER:		20	17	15	18	20	20	15	16	

STOMACH, NONGL (SU)		NUMBER EXAMINED:		20	17	15	18	20	20	15	16	
		NOT REMARKABLE:		20	17	15	18	20	20	15	15	
WALL, THICKENED				0	0	0	0	0	0	0	1	
RAISED AREA				0	0	0	0	0	0	0	1	

DUODENUM (DU)		NUMBER EXAMINED:		20	17	15	18	20	20	15	16	
		NOT REMARKABLE:		20	17	15	18	20	20	15	16	

JEJUNUM (JE)		NUMBER EXAMINED:		20	17	15	18	20	20	15	16	
		NOT REMARKABLE:		20	17	15	18	20	20	15	16	

ILEUM (IL)		NUMBER EXAMINED:		20	17	15	18	20	20	15	16	
		NOT REMARKABLE:		20	17	15	18	20	20	15	16	

CECUM (CE)		NUMBER EXAMINED:		20	17	15	18	20	20	15	16	
		NOT REMARKABLE:		20	17	15	18	19	20	15	15	

DARK AREA				0	0	0	0	1	0	0	1	

COLON (CO)		NUMBER EXAMINED:		20	17	15	18	20	20	15	16	
		NOT REMARKABLE:		20	17	15	18	20	20	15	16	

RECTUM (RE)		NUMBER EXAMINED:		20	17	15	18	20	20	15	16	
		NOT REMARKABLE:		20	17	15	18	20	20	15	16	

TABLE 10A
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

STUDY NUMBER: 2399108

GROSS PATHOLOGY INCIDENCE SUMMARY

		--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---									
TABLE INCLUDES:		SEX:		---MALE---					---FEMALE---		
SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH=T;SUBSET=ALL		GROUP: -1- -2- -3- -4- -1- -2- -3- -4-									
ORGAN AND KEYWORD(S) OR PHRASE		NUMBER: 20 17 15 18 20 20 20 15 16									
LN, MESENTERIC (MS)	NUMBER EXAMINED:	20	17	15	18	20	20	20	15	16	
	NOT REMARKABLE:	20	17	15	18	20	20	20	15	15	
DARK AREA	NUMBER EXAMINED:	0	0	0	0	0	0	0	0	1	
	NOT REMARKABLE:	20	17	15	18	0	0	0	0	0	
TESTIS (TE)	NUMBER EXAMINED:	20	17	15	18	0	0	0	0	0	
	NOT REMARKABLE:	20	16	15	18	0	0	0	0	0	
SOFT PALE CYST	NUMBER EXAMINED:	0	1	0	0	0	0	0	0	0	
	NOT REMARKABLE:	0	1	0	0	0	0	0	0	0	
EPIDIDYMS (EP)	NUMBER EXAMINED:	20	17	15	18	0	0	0	0	0	
	NOT REMARKABLE:	20	17	15	18	0	0	0	0	0	
OVARY (OV)	NUMBER EXAMINED:	0	0	0	0	0	20	20	15	16	
	NOT REMARKABLE:	0	0	0	0	0	20	20	15	16	
UTERUS (UT)	NUMBER EXAMINED:	0	0	0	0	0	20	20	15	16	
	NOT REMARKABLE:	0	0	0	0	0	17	19	13	14	
LUMEN, FLUID	NUMBER EXAMINED:	0	0	0	0	3	1	2	2	2	
	NOT REMARKABLE:	0	0	0	0	0	0	0	0	0	
URINARY BLADDER (UB)	NUMBER EXAMINED:	20	17	15	18	20	20	20	15	16	
	NOT REMARKABLE:	20	17	15	18	20	20	20	15	16	

TABLE 10A

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88
PAGE: 62

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLUDES:		--- NUMBER - OF - ANIMALS - AFFECTED ---											
SEX=ALL; GROUP=ALL; WEEKS=ALL DEATH=T; SUBSET=ALL		SEX:		---MALE---		---FEMALE---							
		GROUP: -1- -2- -3- -4-		-1- -2- -3- -4-									
ORGAN AND KEYWORD(S) OR PHRASE		NUMBER: 20 17 15 18		20 20 20 15 16									
PROSTATE (PR)	NUMBER EXAMINED:	20	17	15	18	0	0	0	0	0	0	0	0
	NOT REMARKABLE:	20	17	14	18	0	0	0	0	0	0	0	0
DARK AREA	NUMBER EXAMINED:	0	0	1	0	0	0	0	0	0	0	0	0
	NOT REMARKABLE:	20	17	15	18	0	0	0	0	0	0	0	0
SEMINAL VESICLE (SV)	NUMBER EXAMINED:	20	17	15	18	0	0	0	0	0	0	0	0
	NOT REMARKABLE:	20	17	15	18	0	0	0	0	0	0	0	0
SKIN (SK)	NUMBER EXAMINED:	20	17	15	18	20	20	20	20	15	16	16	16
	NOT REMARKABLE:	20	17	15	18	20	20	20	20	15	16	16	16
MAMMARY GLAND (MG)	NUMBER EXAMINED:	20	17	15	18	20	20	20	20	15	16	16	16
	NOT REMARKABLE:	20	17	15	18	20	20	20	20	15	16	16	16
MASS-UFL	NUMBER EXAMINED:	0	0	0	0	0	1	0	0	0	0	0	0
	NOT REMARKABLE:	20	17	15	18	20	20	20	20	15	16	16	16
MUSCLE, SKELETAL (SM)	NUMBER EXAMINED:	20	17	15	18	20	20	20	20	15	16	16	16
	NOT REMARKABLE:	20	17	15	18	20	20	20	20	15	16	16	16
EYE (EY)	NUMBER EXAMINED:	20	17	15	18	20	20	20	20	15	16	16	16
	NOT REMARKABLE:	19	16	15	18	19	20	20	20	15	16	16	16
GLOBE RUPTURED POST MORTEM	NUMBER EXAMINED:	1	1	0	0	1	0	0	0	0	0	0	0
	NOT REMARKABLE:	20	17	15	18	20	20	20	20	15	16	16	16
LACRIMAL GL, EXO (EO)	NUMBER EXAMINED:	20	17	15	18	20	20	20	20	15	16	16	16
	NOT REMARKABLE:	20	17	15	18	20	20	20	20	15	16	16	16

TABLE 18A
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=T;SUBSET=ALL

SEX: ---MALE--- ---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 20 17 15 18 20 20 20 15 16

ORGAN AND KEYWORD(S) OR PHRASE

BONE, STERNUM (SB) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

MARROW, STERNUM (SE) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

BONE, FEMUR (FE) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

SKIN, OTHER (SS) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

LN, OTHER (LN) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 20 17 15 18 20 20 20 15 16

COLLECTED/TAKEN (XM) NUMBER EXAMINED: 20 17 15 18 20 20 20 15 16
NOT REMARKABLE: 15 7 5 8 15 10 6 6

ELECTRON MICROSCOPY SAMPLE
5 10 10 10 5 10 9 10

** END OF LIST **

TABLE 10B

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=UNSCHED;SUBSET=T

SEX: -----MALE-----FEMALE-----

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 5 4

ORGAN AND KEYWORD(S) OR PHRASE

** TOP OF LIST **

BRAIN W/STEM (BR)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 1 4 2 0 0 5 4

SOFT

0 2 1 0 0 0 0 0

PITUITARY (PI)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 3 5 2 0 0 5 4

CORD, CERVICAL (CS)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 3 5 2 0 0 5 4

CORD, THORACIC (TC)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 3 5 2 0 0 5 4

CORD, LUMBAR (LC)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 3 5 2 0 0 5 4

NERVE, SCIATIC (SN)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 3 5 2 0 0 5 4

LUNG (LU)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 1 0 0 0 0 0 0

FAILURE TO COLLAPSE
MOTTLED

0 2 5 2 0 0 5 4

0 0 0 5 2 0 0 5

TABLE 10B
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

--- NUMBER - OF - ANIMALS - AFFECTED ---

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=UNSCHED;SUBSET=T

SEX: ---MALE---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 0 5 4

ORGAN AND KEYWORD(S) OR PHRASE

KIDNEY (KD) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

ADRENAL, MEDULLA (AM) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

ADRENAL, CORTEX (AC) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

LIVER (LI) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 2 5 2 0 0 0 5 4

H-ENLARGED
SPLEEN (SP) NUMBER EXAMINED: 0 1 0 0 0 0 0 0 0
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

PANCREAS (PA) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

HEART (HT) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

THYMS (TH) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLUDES:
SEX=ALL; GROUP=ALL; WEEKS=ALL
DEATH=UNSCHED; SUBSET=T

--- NUMBER OF ANIMALS - AFFECTED ---

SEX: ---MALE---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 0 5 4

ORGAN AND KEYWORD(S) OR PHRASE

TRACHEA (TR) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

THYROID (TY) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

PARATHYROID (PT) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

ESOPHAGUS (ES) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

MAND SALIVARY GL (SG) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

AORTA, THORACIC (AO) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

STOMACH, GL (ST) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 1 0 0 0 5 4

PALE AREA

STOMACH, NONGL (SU) NUMBER EXAMINED: 0 0 0 1 0 0 0 0 0
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

TABLE 10B
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=UNSCHED;SUBSET=T

SEX: ---MALE--- ---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 0 5 4

ORGAN AND KEYWORD(S) OR PHRASE

DUODENUM (DU) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

JEJUNUM (JE) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

ILEUM (IL) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

CECUM (CE) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

COLON (CO) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

RECTUM (RE) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

LN, MESENTERIC (MS) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

TESTIS (TE) NUMBER EXAMINED: 0 3 5 2 0 0 0 0 0
NOT REMARKABLE: 0 3 4 2 0 0 0 0 0

UNEQUALLY SIZED

TABLE INCLUDES:		--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---									
SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH=UNSCHED;SUBSET=T		SEX:		MALE		FEMALE					
GROUP:		-1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-		
NUMBER:		0	3	5	2	0	0	0	5	4	
ORGAN AND KEYWORD(S) OR PHRASE											
EPIDIDYMIS (EP)	NUMBER EXAMINED:	0	3	5	2	0	0	0	0	0	0
	NOT REMARKABLE:	0	3	5	2	0	0	0	0	0	0
OVARY (OV)	NUMBER EXAMINED:	0	0	0	0	0	0	0	5	4	
	NOT REMARKABLE:	0	0	0	0	0	0	0	5	4	
UTERUS (UT)	NUMBER EXAMINED:	0	0	0	0	0	0	0	5	4	
	NOT REMARKABLE:	0	0	0	0	0	0	0	5	4	
URINARY BLADDER (UB)	NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4	
	NOT REMARKABLE:	0	3	5	2	0	0	0	5	4	
PROSTATE (PR)	NUMBER EXAMINED:	0	3	5	2	0	0	0	0	0	
	NOT REMARKABLE:	0	3	5	2	0	0	0	0	0	
SEMINAL VESICLE (SV)	NUMBER EXAMINED:	0	3	5	2	0	0	0	0	0	
	NOT REMARKABLE:	0	3	5	2	0	0	0	0	0	
SKIN (SK)	NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4	
	NOT REMARKABLE:	0	3	5	2	0	0	0	5	4	
MAMMARY GLAND (MG)	NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4	
	NOT REMARKABLE:	0	3	5	2	0	0	0	5	4	

STUDY NUMBER: 2399108

TABLE 10B
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

GROSS PATHOLOGY INCIDENCE SUMMARY

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=UNSCHED;SUBSET=T

SEX: ---MALE---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 0 5 4

ORGAN AND KEYWORD(S) OR PHRASE

MUSCLE, SKELETAL (SM) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

EYE (EY) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

LACRIMAL GL, EXO (EO) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 3

DARK AREA
0 0 0 0 0 0 0 0 1

BONE, STERNUM (SB) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

MARROW, STERNUM (SE) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

BONE, FEMUR (FE) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

SKIN, OTHER (SS) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 2 5 2 0 0 0 5 4

SORE
0 1 0 0 0 0 0 0 0

TABLE 10B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

--- NUMBER - OF - ANIMALS - AFFECTED ---

TABLE INCLUDES:

SEX=ALL;GROUP=ALL;WEEKS=ALL
DEATH=UNSCHED;SUBSET=T

SEX: ---MALE---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

ORGAN AND KEYWORD(S) OR PHRASE

NUMBER: 0 3 5 2 0 0 5 4

LN, OTHER (LN)

NUMBER EXAMINED: 0 3 5 2 0 0 5 4

NOT REMARKABLE: 0 2 5 2 0 0 5 4

ENLARGED

** END OF LIST **

0 1 0 0 0 0 0 0

HISTOPATHOLOGY INCIDENCE SUMMARY

--- NUMBER - DF - ANIMALS - AFFECTED ---

TABLE INCLUDES:											
SEX=ALL; GROUP=ALL; SCREEN=ALL; WEEKS=ALL											
DEATH=T; FIND=ALL; SUBSET=ALL											
SEX: -----MALE-----FEMALE-----											
GROUP: -1- -2- -3- -4- -1- -2- -3- -4-											
NUMBER: 20 17 15 18 20 20 15 16											
ORGAN AND FINDING DESCRIPTION											
** TDP OF LIST **											
BRAIN W/STEM (BR) NUMBER EXAMINED: 20 0 0 18 20 0 0 16											
NOT REMARKABLE: 20 0 0 18 20 0 0 16											
PITUITARY (PI) NUMBER EXAMINED: 20 0 0 18 19 0 0 16											
NOT REMARKABLE: 20 0 0 18 18 0 0 16											
--CYST											
0 0 0 0 1 0 0 0											
CORD, CERVICAL (CS) NUMBER EXAMINED: 20 0 0 18 20 0 0 16											
NOT REMARKABLE: 20 0 0 18 20 0 0 16											
CORD, THORACIC (TC) NUMBER EXAMINED: 20 0 0 18 20 0 0 16											
NOT REMARKABLE: 20 0 0 18 20 0 0 16											
CORD, LUMBAR (LC) NUMBER EXAMINED: 20 0 0 18 20 0 0 16											
NOT REMARKABLE: 20 0 0 18 20 0 0 16											
ADRENAL, MEDULLA (AM) NUMBER EXAMINED: 20 0 0 18 20 0 0 16											
NOT REMARKABLE: 20 0 0 18 20 0 0 15											
--UNILATERALLY EXAMINED											
0 0 0 0 0 0 0 1											
ADRENAL, CORTEX (AC) NUMBER EXAMINED: 20 0 0 18 20 0 0 16											
NOT REMARKABLE: 17 0 0 18 19 0 0 16											
--VACUOLIZATION											
3 0 0 0 0 0 0 0											
--DEGENERATION											
0 0 0 0 1 0 0 0											

HISTOPATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLUDES:												
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL												
DEATH=T;FIND=ALL;SUBSET=ALL												
--- NUMBER - OF - ANIMALS - AFFECTED ---												
SEX: -----MALE-----FEMALE-----												
GROUP: -1- -2- -3- -4- -1- -2- -3- -4-												
NUMBER: 20 17 15 18 20 20 15 16												
ORGAN AND FINDING DESCRIPTION												
TRACHEA (TR)	NUMBER EXAMINED:	20	0	0	18	20	0	0	16			
	NOT REMARKABLE:	20	0	0	18	20	0	0	16			
THYROID (TY)	NUMBER EXAMINED:	20	0	0	18	20	0	0	16			
	NOT REMARKABLE:	20	0	0	18	20	0	0	16			
PARATHYROID (PT)	NUMBER EXAMINED:	12	0	0	12	12	0	0	15			
	NOT REMARKABLE:	12	0	0	12	12	0	0	15			
ESOPHAGUS (ES)	NUMBER EXAMINED:	20	0	0	18	20	0	0	16			
	NOT REMARKABLE:	20	0	0	18	20	0	0	16			
LUNG (LU)	NUMBER EXAMINED:	20	17	15	18	20	20	15	16			
	NOT REMARKABLE:	0	0	0	1	0	0	1	0			
--PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID --FOREIGN MATERIAL --PNEUMONITIS	20	17	15	17	20	20	14	16				
	0	0	1	0	0	0	0	0				
	0	1	0	0	3	1	0	0				
HEART (HT)	NUMBER EXAMINED:	20	0	0	18	20	0	1	16			
	NOT REMARKABLE:	15	0	0	18	20	0	1	16			
--CARDIOMYOPATHY, DEGENERATIVE												
SPLEEN (SP)	NUMBER EXAMINED:	20	0	0	18	20	0	0	16			
	NOT REMARKABLE:	20	0	0	18	20	0	0	16			

TABLE 11A
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
HISTOPATHOLOGY INCIDENCE SUMMARY

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

STUDY NUMBER: 2399108

--- NUMBER OF ANIMALS - AFFECTED ---

SEX: ---MALE--- ---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 20 17 15 18 20 20 15 16

ORGAN AND FINDING DESCRIPTION

LIVER (LI) NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 13 14 13 13 12 12 12 12

--FOCI OF MONONUCLEAR CELLS
--FOCAL HEPATITIS
--BILE DUCT, INFLAMMATION, CHRONIC
--(MULTI)FOCAL NECROSIS
--INJECTION SITE

KIDNEY (KD) NUMBER EXAMINED: 20 17 15 18 20 20 15 16
NOT REMARKABLE: 14 8 6 10 17 14 10 14

--NEPHROPATHY, CHRONIC PROGRESSIVE
--TUBULE, MICROCONCRETION
--PELVIS, DILATATION
--GRANULAR CASTS
--PYELONEPHRITIS
--CORTICAL CYST

STOMACH, GL (ST) NUMBER EXAMINED: 20 0 0 18 20 0 1 16
NOT REMARKABLE: 20 0 0 18 20 0 0 16

--CONGESTION

STOMACH, NONGL (SU) NUMBER EXAMINED: 20 0 0 18 20 0 0 16
NOT REMARKABLE: 20 0 0 18 20 0 0 15

--ACANTHOSIS
--INFLAMMATION, CHRONIC

DUODENUM (DU) NUMBER EXAMINED: 20 0 0 18 20 0 0 16
NOT REMARKABLE: 20 0 0 18 20 0 0 16

TABLE 11A
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
HISTOPATHOLOGY INCIDENCE SUMMARY

PRINTED: 22-APR-88
PAGE: 74

STUDY NUMBER: 2399108

TABLE INCLUDES:		--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---									
SEX=ALL; GROUP=ALL; SCREEN=ALL; WEEKS=ALL		SEX:	MALE				FEMALE				
DEATH=T; FIND=ALL; SUBSET=ALL		GROUP:	-1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-	
ORGAN AND FINDING DESCRIPTION		NUMBER:	20	17	15	18	20	20	15	16	
JEJUNUM (JE)		NUMBER EXAMINED:	20	0	0	18	20	0	0	15	
		NOT REMARKABLE:	20	0	0	18	20	0	0	15	
ILEUM (IL)		NUMBER EXAMINED:	20	0	0	18	20	0	0	16	
		NOT REMARKABLE:	20	0	0	18	20	0	0	16	
PANCREAS (PA)		NUMBER EXAMINED:	20	0	0	18	20	0	0	16	
		NOT REMARKABLE:	18	0	0	18	20	0	0	16	
--INFLAMMATION, CHRONIC			2	0	0	0	0	0	0	0	
CECUM (CE)		NUMBER EXAMINED:	20	0	0	18	20	0	0	16	
		NOT REMARKABLE:	20	0	0	18	19	0	0	16	
--INJECTION SITE			0	0	0	0	1	0	0	0	
COLON (CO)		NUMBER EXAMINED:	20	0	0	18	20	0	0	16	
		NOT REMARKABLE:	20	0	0	18	20	0	0	16	
RECTUM (RE)		NUMBER EXAMINED:	20	0	0	18	20	0	0	16	
		NOT REMARKABLE:	20	0	0	18	20	0	0	16	
LN, MESENTERIC (MS)		NUMBER EXAMINED:	20	0	0	18	20	0	0	16	
		NOT REMARKABLE:	20	0	0	18	20	0	0	15	
--CONGESTION			0	0	0	0	0	0	0	1	

HISTOPATHOLOGY INCIDENCE SUMMARY

--- NUMBER - OF - ANIMALS - AFFECTED ---

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=T;FIND=ALL;SUBSET=ALL

SEX: ---MALE--- ---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 20 17 15 18 20 20 15 16

ORGAN AND FINDING DESCRIPTION

TESTIS (TE) NUMBER EXAMINED: 20 1 0 18 0 0 0 0
NOT REMARKABLE: 19 0 0 18 0 0 0 0

--DEGENERATION

EPIDIDYMIS (EP) NUMBER EXAMINED: 20 0 0 18 0 0 0 0
NOT REMARKABLE: 20 0 0 18 0 0 0 0

Ovary (OV)

NUMBER EXAMINED: 0 0 0 0 20 0 0 16
NOT REMARKABLE: 0 0 0 0 19 0 0 16

--UNILATERALLY EXAMINED

UTERUS (UT) NUMBER EXAMINED: 0 0 0 0 20 1 2 16
NOT REMARKABLE: 0 0 0 0 15 0 0 10

--DILATATION

URINARY BLADDER (UB) NUMBER EXAMINED: 20 0 0 17 20 0 0 16
NOT REMARKABLE: 20 0 0 16 20 0 0 16

--CALCULUS

--MUCOSAL HYPERPLASIA

PROSTATE (PR) NUMBER EXAMINED: 20 0 1 10 0 0 0 0
NOT REMARKABLE: 20 0 1 16 0 0 0 0

--INFLAMMATION, CHRONIC ACTIVE
--MONONUCLEAR CELL INFILTRATE

0 0 0 1 0 0 0 0
0 0 0 1 0 0 0 0

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=T;FIND=ALL;SUBSET=ALL

SEX: ---MALE--- ---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 20 17 15 18 20 20 15 16

ORGAN AND FINDING DESCRIPTION

SEMINAL VESICLE (SV) NUMBER EXAMINED: 20 0 0 18 0 0 0 0
NOT REMARKABLE: 20 0 0 17 0 0 0 0

--INFLAMMATION, CHRONIC ACTIVE

SKIN (SK) NUMBER EXAMINED: 20 0 0 18 20 0 0 16
NOT REMARKABLE: 20 0 0 18 20 0 0 16

MAMMARY GLAND (MG)

..... NUMBER EXAMINED: 18 0 0 13 20 1 0 14
NOT REMARKABLE: 18 0 0 13 20 0 0 14

--M-ADENOCARCINOMA

MUSCLE, SKELETAL (SM) NUMBER EXAMINED: 20 0 0 18 20 0 0 16
NOT REMARKABLE: 20 0 0 18 20 0 0 16

NERVE, SCIATIC (SN)

..... NUMBER EXAMINED: 20 0 0 18 20 0 0 16
NOT REMARKABLE: 20 0 0 18 20 0 0 16

MAND SALIVARY GL (SG)

..... NUMBER EXAMINED: 20 0 0 18 20 0 0 16
NOT REMARKABLE: 20 0 0 18 20 0 0 16

THYMUS (TH)

..... NUMBER EXAMINED: 19 0 0 18 20 0 0 16
NOT REMARKABLE: 19 0 0 18 20 0 0 16

AORTA, THORACIC (AO)

..... NUMBER EXAMINED: 20 0 0 18 20 0 0 16
NOT REMARKABLE: 20 0 0 18 20 0 0 16

TABLE 11A
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
HISTOPATHOLOGY INCIDENCE SUMMARY

SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=T;FIND=ALL;SUBSET=ALL

STUDY NUMBER: 2399108

PRINTED: 22-APR-88

PAGE: 77

--- NUMBER OF ANIMALS - AFFECTED ---

SEX: ---MALE--- ---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-
NUMBER: 20 17 15 18 20 20 15 16

ORGAN AND FINDING DESCRIPTION

EYE (EY)	NUMBER EXAMINED: 20	1	0	18	20	0	0	0	16
	NOT REMARKABLE: 13	1	0	17	18	0	0	13	
--CHRONIC INFLAMMATION, HARDERIAN GLAND		6	0	0	1	2	0	0	3
--ONE EXAMINED		1	0	0	0	0	0	0	0
LACRIMAL GL, EXO (EO)	NUMBER EXAMINED: 20	1	0	18	20	0	0	16	
	NOT REMARKABLE: 17	1	0	18	20	0	0	16	
--FOCAL MONONUCLEAR INFILTRATE		3	0	0	0	0	0	0	0
BONE, STERNUM (SB)	NUMBER EXAMINED: 20	0	0	18	20	0	0	16	
	NOT REMARKABLE: 20	0	0	18	20	0	0	16	
MARROW, STERNUM (SE)	NUMBER EXAMINED: 20	0	0	18	20	0	0	16	
	NOT REMARKABLE: 20	0	0	17	20	0	0	16	
--HYPERCELLULAR		0	0	0	1	0	0	0	0
BONE, FEMUR (FE)	NUMBER EXAMINED: 20	0	0	18	20	0	0	16	
	NOT REMARKABLE: 19	0	0	16	20	0	0	14	
--ARTICULAR SURFACE NOT PRESENT		1	0	0	2	0	0	0	2
LN, OTHER (LN)	NUMBER EXAMINED: 0	0	0	0	0	0	0	0	0
	NOT REMARKABLE: 0	0	0	0	0	0	0	0	0
SKIN, OTHER (SS)	NUMBER EXAMINED: 0	0	0	0	0	0	0	0	0
	NOT REMARKABLE: 0	0	0	0	0	0	0	0	0

** END OF LIST **

TABLE INCLUDES:
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=UNSCHED;FIND=ALL;SUBSET=ALL

		--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---									
		SEX: ---MALE---					---FEMALE---				
		GROUP: -1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-		
		NUMBER:	0	3	5	2	0	0	5	4	
ORGAN AND FINDING DESCRIPTION											
** TOP OF LIST **											
BRAIN W/STEM (BR)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	3	5	2	0	0	5	4	
PITUITARY (PI)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	3	5	2	0	0	5	4	
CORD, CERVICAL (CS)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	3	5	2	0	0	5	4	
CORD, THORACIC (TC)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	3	5	2	0	0	5	4	
CORD, LUMBAR (LC)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	3	5	2	0	0	5	4	
ADRENAL, MEDULLA (AM)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	2	4	2	0	0	5	3	
--UNILATERALLY EXAMINED			0	1	1	0	0	0	0	1	
ADRENAL, CORTEX (AC)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	3	4	2	0	0	5	4	
--UNILATERALLY EXAMINED			0	0	1	0	0	0	0	0	
TRACHEA (TR)		NUMBER EXAMINED:	0	3	5	2	0	0	5	4	
		NOT REMARKABLE:	0	3	5	2	0	0	5	4	

HISTOPATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLUDES:		--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---									
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=UNSCHED;FIND=ALL;SUBSET=ALL		SEX:	-----MALE-----		-----FEMALE-----						
		GROUP:	-1-	-2-	-3-	-4-	-1-	-2-	-3-	-4-	
ORGAN AND FINDING DESCRIPTION		NUMBER:	0	3	5	2	0	0	0	5	4
THYROID (TY)		NUMBER EXAMINED:	0	3	4	2	0	0	0	5	4
		NOT REMARKABLE:	0	3	4	2	0	0	0	5	4
PARATHYROID (PT)		NUMBER EXAMINED:	0	3	3	2	0	0	0	5	2
		NOT REMARKABLE:	0	3	3	2	0	0	0	5	2
ESOPHAGUS (ES)		NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4
		NOT REMARKABLE:	0	3	5	2	0	0	0	5	4
LUNG (LU)		NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4
		NOT REMARKABLE:	0	1	0	0	0	0	0	0	0
--PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID			0	2	4	1	0	0	0	5	2
--FOREIGN BODY PNEUMONIA			0	0	0	1	0	0	0	0	0
--CONGESTION			0	0	1	1	0	0	0	0	0
--FOREIGN MATERIAL			0	2	4	1	0	0	0	5	4
--EDEMA			0	0	0	0	0	0	0	0	2
HEART (HT)		NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4
		NOT REMARKABLE:	0	3	5	2	0	0	0	5	4
SPLEEN (SP)		NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4
		NOT REMARKABLE:	0	3	5	2	0	0	0	5	4
LIVER (LI)		NUMBER EXAMINED:	0	3	5	2	0	0	0	5	4
		NOT REMARKABLE:	0	2	5	2	0	0	0	5	4
--FOCI OF MONONUCLEAR CELLS			0	1	0	0	0	0	0	0	0

--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---									
TABLE INCLUDES:									
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL									
DEATH=UNSCHED;FIND=ALL;SUBSET=ALL									
SEX: -----MALE-----FEMALE-----									
GROUP: -1- -2- -3- -4- -1- -2- -3- -4-									
NUMBER: 0 3 5 2 0 0 0 5 4									
ORGAN AND FINDING DESCRIPTION									
KIDNEY (KD)									
NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4									
NOT REMARKABLE: 0 3 5 2 0 0 0 4 4									
--NEPHROPATHY, CHRONIC PROGRESSIVE									
--PELVIS, DILATATION									
STOMACH, GL (ST)									
NUMBER EXAMINED: 0 3 4 2 0 0 0 5 4									
NOT REMARKABLE: 0 3 4 2 0 0 0 5 4									
STOMACH, NONGL (SU)									
NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4									
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4									
DUODENUM (DU)									
NUMBER EXAMINED: 0 2 3 2 0 0 0 5 3									
NOT REMARKABLE: 0 2 3 2 0 0 0 5 3									
JEJUNUM (JE)									
NUMBER EXAMINED: 0 2 3 2 0 0 0 5 3									
NOT REMARKABLE: 0 2 3 2 0 0 0 5 3									
ILEUM (IL)									
NUMBER EXAMINED: 0 2 2 2 0 0 0 5 3									
NOT REMARKABLE: 0 2 2 2 0 0 0 5 3									
PANCREAS (PA)									
NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4									
NOT REMARKABLE: 0 3 5 1 0 0 0 5 4									
--INFLAMMATION, CHRONIC									
NUMBER EXAMINED: 0 0 0 1 0 0 0 0 0									
NOT REMARKABLE: 0 0 0 1 0 0 0 0 0									

TABLE 118
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
HISTOPATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

--- NUMBER OF ANIMALS - AFFECTED ---

TABLE INCLUDES: SEX: ---MALE---FEMALE---

SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=UNSCHED;FIND=ALL;SUBSET=ALL

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 5 4

ORGAN AND FINDING DESCRIPTION

CECUM (CE) NUMBER EXAMINED: 0 2 3 2 0 0 5 3
NOT REMARKABLE: 0 2 3 2 0 0 5 3

COLON (CO) NUMBER EXAMINED: 0 2 3 2 0 0 5 3
NOT REMARKABLE: 0 2 3 2 0 0 5 3

RECTUM (RE) NUMBER EXAMINED: 0 2 3 2 0 0 4 3
NOT REMARKABLE: 0 2 3 2 0 0 4 3

LN, MESENTERIC (MS) NUMBER EXAMINED: 0 3 5 2 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 5 4

TESTIS (TE) NUMBER EXAMINED: 0 3 5 2 0 0 0 0
NOT REMARKABLE: 0 3 5 2 0 0 0 0

EPIDIDYMIS (EP) NUMBER EXAMINED: 0 3 5 2 0 0 0 0
NOT REMARKABLE: 0 3 5 2 0 0 0 0

OVARY (OV) NUMBER EXAMINED: 0 0 0 0 0 0 5 4
NOT REMARKABLE: 0 0 0 0 0 0 5 4

UTERUS (UT) NUMBER EXAMINED: 0 0 0 0 0 0 5 4
NOT REMARKABLE: 0 0 0 0 0 0 5 4

TABLE INCLUDES: SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=UNSCHED;FIND=ALL;SUBSET=ALL

SEX: ---MALE---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 0 5 4

ORGAN AND FINDING DESCRIPTION

URINARY BLADDER (UB) NUMBER EXAMINED: 0 3 4 2 0 0 0 5 4
NOT REMARKABLE: 0 3 4 2 0 0 0 5 4

PROSTATE (PR) NUMBER EXAMINED: 0 3 5 2 0 0 0 0 0
NOT REMARKABLE: 0 2 4 2 0 0 0 0 0

--MONONUCLEAR CELL INFILTRATE

SEMINAL VESICLE (SV) NUMBER EXAMINED: 0 3 5 2 0 0 0 0 0
NOT REMARKABLE: 0 3 5 2 0 0 0 0 0

SKIN (SK) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

MAMMARY GLAND (MG) NUMBER EXAMINED: 0 1 4 1 0 0 0 5 3
NOT REMARKABLE: 0 1 4 1 0 0 0 5 3

MUSCLE, SKELETAL (SM) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

NERVE, SCIATIC (SN) NUMBER EXAMINED: 0 2 5 2 0 0 0 5 4
NOT REMARKABLE: 0 2 5 2 0 0 0 5 4

MAND SALIVARY GL (SG) NUMBER EXAMINED: 0 3 5 2 0 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 0 5 4

--- NUMBER - OF - ANIMALS - AFFECTED ---

HISTOPATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLUDES: SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=UNSCHED;FIND=ALL;SUBSET=ALL

SEX: ---MALE---FEMALE---

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 5 4

ORGAN AND FINDING DESCRIPTION

THYMUS (TH) NUMBER EXAMINED: 0 3 5 2 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 5 4

AORTA, THORACIC (AO) NUMBER EXAMINED: 0 2 5 2 0 0 5 4
NOT REMARKABLE: 0 2 5 2 0 0 5 4

EYE (EY) NUMBER EXAMINED: 0 3 4 2 0 0 4 4
NOT REMARKABLE: 0 3 4 2 0 0 4 4

LACRIMAL GL, EXO (EO) NUMBER EXAMINED: 0 3 5 2 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 5 4

BONE, STERNUM (SB) NUMBER EXAMINED: 0 3 5 2 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 5 4

MARROW, STERNUM (SE) NUMBER EXAMINED: 0 3 5 2 0 0 5 4
NOT REMARKABLE: 0 3 5 2 0 0 5 4

BONE, FEMUR (FE) NUMBER EXAMINED: 0 3 5 2 0 0 5 4
NOT REMARKABLE: 0 2 5 2 0 0 4 3

--ARTICULAR SURFACE NOT PRESENT

LN, OTHER (LN) NUMBER EXAMINED: 0 1 0 0 0 0 0 0
NOT REMARKABLE: 0 0 0 0 0 0 0 0

--HYPERPLASIA, LYMPHOID

0 1 0 0 0 0 0 0

TABLE 11B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88
PAGE: 84

HISTOPATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLUDES:

FILE INCLUDES:
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=UNSCHED;FIND=ALL;SUBSET=ALL

--- NUMBER-OF-ANIMALS-AFFECTED ---

SEX: -----MALE-----FEMALE-----

GROUP: -1- -2- -3- -4- -1- -2- -3- -4-

NUMBER: 0 3 5 2 0 0 5 4

ORGAN AND FINDING DESCRIPTION

[illegible]

```

--INFLAMMATION, GRANULOMATOUS
** END OF LIST **

```




HAZLETON

LABORATORIES AMERICA, INC.

1330 - B PICCARO DRIVE, ROCKVILLE, MARYLAND 20850

HLA 2399-108

- 85 -

APPENDIX 1

Individual Animal Disposition

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL DISPOSITION

ANIMAL-NUMBER (PIN)	DOSE GROUP	SEX	TERMINAL BODY WEIGHT	DEATH CODE	TYPE OF DEATH	DESCRIPTION OF DEATH	DATE OF DEATH	DAY OF STUDY	WEEK OF STUDY
B08362	1	MALE	563.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08363	1	MALE	452.7	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08364	1	MALE	543.3	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08365	1	MALE	605.9	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08366	1	MALE	457.0	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08367	1	MALE	451.7	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08368	1	MALE	511.3	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08369	1	MALE	508.4	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08370	1	MALE	459.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08371	1	MALE	493.7	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08372	1	MALE	487.8	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08373	1	MALE	588.4	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08374	1	MALE	524.3	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08375	1	MALE	459.3	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08376	1	MALE	518.8	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08377	1	MALE	492.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08378	1	MALE	494.7	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08379	1	MALE	554.1	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08380	1	MALE	479.0	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08381	1	MALE	265.5	M	UNSCHEDULED	UNSCHEDULED DEATH	04/23/86	13	2
B08402	2	MALE	516.3	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08403	2	MALE	512.3	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08404	2	MALE	492.8	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08405	2	MALE	515.8	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08406	2	MALE	481.6	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08407	2	MALE	473.1	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08408	2	MALE	471.7	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08409	2	MALE	492.8	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08410	2	MALE	575.0	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08411	2	MALE	527.4	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08412	2	MALE	506.0	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08413	2	MALE	528.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08414	2	MALE	460.6	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08415	2	MALE	425.6	D	UNSCHEDULED	UNSCHEDULED DEATH	05/14/86	34	5
B08416	2	MALE	305.5	D	UNSCHEDULED	UNSCHEDULED DEATH	04/25/86	15	3
B08417	2	MALE	225.9	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08418	2	MALE	499.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08419	2	MALE	443.2	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08420	2	MALE		T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14

HAZLETON LABORATORIES AMERICA, INC.
 DEPARTMENT OF PATHOLOGY

PRINTED: 22-APR-88
 PAGE: 87

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL DISPOSITION

ANIMAL-NUMBER (PIN)	DOSE GROUP	SEX	TERMINAL BODY WEIGHT	DEATH CODE	TYPE OF DEATH	DESCRIPTION OF DEATH	DATE OF DEATH	DAY OF STUDY	WEEK OF STUDY
B08421	2	MALE	414.5	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08442	3	MALE	452.4	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08443	3	MALE	481.1	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08444	3	MALE	500.0	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08445	3	MALE	455.1	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08446	3	MALE	316.7	D	UNSCHEDULED	UNSCHEDULED DEATH	04/30/86	20	3
B08447	3	MALE	468.5	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08448	3	MALE	362.4	D	UNSCHEDULED	UNSCHEDULED DEATH	05/14/86	34	5
B08449	3	MALE	423.1	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08450	3	MALE	450.8	D	UNSCHEDULED	UNSCHEDULED DEATH	05/31/86	51	8
B08451	3	MALE	449.8	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08452	3	MALE	433.6	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08453	3	MALE	439.0	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08454	3	MALE	333.8	D	UNSCHEDULED	UNSCHEDULED DEATH	04/29/86	19	3
B08455	3	MALE	463.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08456	3	MALE	495.9	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08457	3	MALE	530.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08458	3	MALE	216.1	D	UNSCHEDULED	UNSCHEDULED DEATH	04/14/86	4	1
B08459	3	MALE	495.7	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08460	3	MALE	495.7	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08461	3	MALE	503.6	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08482	4	MALE	466.3	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08483	4	MALE	452.5	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08484	4	MALE	651.8	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08485	4	MALE	359.5	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08486	4	MALE	444.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08487	4	MALE	431.0	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08488	4	MALE	374.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08489	4	MALE	373.1	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08490	4	MALE	405.0	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08491	4	MALE	287.1	D	UNSCHEDULED	UNSCHEDULED DEATH	06/05/86	56	8
B08492	4	MALE	435.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08493	4	MALE	317.0	D	UNSCHEDULED	UNSCHEDULED DEATH	04/27/86	17	3
B08494	4	MALE	415.0	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08495	4	MALE	406.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08496	4	MALE	444.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08497	4	MALE	449.7	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08498	4	MALE	451.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08499	4	MALE	433.5	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14

INDIVIDUAL ANIMAL DISPOSITION

ANIMAL-NUMBER (PIN)	DDSE GROUP	SEX	TERMINAL BODY WEIGHT	DEATH CODE	TYPE DF DEATH	DESCRIPTION DF DEATH	DATE OF DEATH	DAY DF STUDY	WEEK OF STUDY
B08500	4	MALE	443.4	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08501	4	MALE	428.0	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08382	1	FEMALE	278.5	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08383	1	FEMALE	247.1	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08384	1	FEMALE	297.1	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08385	1	FEMALE	262.4	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08386	1	FEMALE	243.6	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08387	1	FEMALE	257.0	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	96	14
B08388	1	FEMALE	251.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08389	1	FEMALE	267.0	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08390	1	FEMALE	261.7	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08391	1	FEMALE	277.8	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08392	1	FEMALE	294.7	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08393	1	FEMALE	266.0	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	96	14
B08394	1	FEMALE	242.5	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	96	14
B08395	1	FEMALE	269.5	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08396	1	FEMALE	248.6	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08397	1	FEMALE	271.1	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08398	1	FEMALE	225.8	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08399	1	FEMALE	290.1	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08400	1	FEMALE	248.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08401	1	FEMALE	262.3	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08422	2	FEMALE	260.3	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08423	2	FEMALE	259.0	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08424	2	FEMALE	272.9	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08425	2	FEMALE	261.3	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08426	2	FEMALE	236.1	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08427	2	FEMALE	275.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08428	2	FEMALE	275.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08429	2	FEMALE	286.6	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08430	2	FEMALE	229.7	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08431	2	FEMALE	257.3	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08432	2	FEMALE	254.6	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	97	14
B08433	2	FEMALE	265.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08434	2	FEMALE	243.1	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08435	2	FEMALE	241.5	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08436	2	FEMALE	257.5	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08437	2	FEMALE	243.2	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08438	2	FEMALE	277.4	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL DISPOSITION

ANIMAL-NUMBER (PIN)	DOSE GROUP	SEX	TERMINAL BODY WEIGHT	DEATH CODE	TYPE OF DEATH	DESCRIPTION OF DEATH	DATE OF DEATH	DAY OF STUDY	WEEK OF STUDY
B08439	2	FEMALE	261.4	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08440	2	FEMALE	253.9	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08441	2	FEMALE	254.6	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08462	3	FEMALE	247.8	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08463	3	FEMALE	236.6	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08464	3	FEMALE	239.5	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08465	3	FEMALE	249.3	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08466	3	FEMALE	280.5	D	UNSCHEDULED	UNSCHEDULED DEATH	07/07/86	88	13
B08467	3	FEMALE	257.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08468	3	FEMALE	201.3	D	UNSCHEDULED	UNSCHEDULED DEATH	04/28/86	18	3
B08469	3	FEMALE	258.1	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08470	3	FEMALE	236.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08471	3	FEMALE	249.4	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08472	3	FEMALE	290.1	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08473	3	FEMALE	165.7	D	UNSCHEDULED	UNSCHEDULED DEATH	04/18/86	8	2
B08474	3	FEMALE	249.0	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08475	3	FEMALE	258.1	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08476	3	FEMALE	269.2	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08477	3	FEMALE	275.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08478	3	FEMALE	180.2	D	UNSCHEDULED	UNSCHEDULED DEATH	04/20/86	18	2
B08479	3	FEMALE	242.1	D	UNSCHEDULED	UNSCHEDULED DEATH	07/15/86	96	14
B08480	3	FEMALE	257.7	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08481	3	FEMALE	259.0	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08502	4	FEMALE	259.9	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08503	4	FEMALE	235.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08504	4	FEMALE	228.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08505	4	FEMALE	175.2	D	UNSCHEDULED	UNSCHEDULED DEATH	04/21/86	11	2
B08506	4	FEMALE	230.9	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08507	4	FEMALE	258.4	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08508	4	FEMALE	233.2	T	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	14
B08509	4	FEMALE	227.0	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08510	4	FEMALE	211.9	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08511	4	FEMALE	242.2	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08512	4	FEMALE	265.8	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08513	4	FEMALE	236.4	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08514	4	FEMALE	251.9	D	UNSCHEDULED	UNSCHEDULED DEATH	06/20/86	71	11
B08515	4	FEMALE	178.0	D	UNSCHEDULED	UNSCHEDULED DEATH	04/20/86	10	2
B08516	4	FEMALE	265.2	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08517	4	FEMALE	223.0	T	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14

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DEPARTMENT OF PATHOLOGY

APPENDIX 1
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88
PAGE: 90

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL DISPOSITION

ANIMAL-NUMBER (PIN)	ANIMAL-NUMBER (HAN)	DOSE GROUP	SEX	TERMINAL BODY WEIGHT	DEATH CODE	TYPE OF DEATH	DESCRIPTION OF DEATH	DATE OF DEATH	DAY OF STUDY	WEEK OF STUDY
B08518	864038	4	FEMALE	239.8	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08519	864039	4	FEMALE	284.1	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
B08520	864040	4	FEMALE	214.2	D	UNSCHEDULED	UNSCHEDULED DEATH	05/29/86	49	7
B08521	864041	4	FEMALE	258.6	T	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14



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HLA 2399-108

- 91 -

APPENDIX 2

Individual Clinical Observations

APPENDIX 2
INDIVIDUAL CLINICAL OBSERVATIONS
2399-108

WEEK	GROUP & SEX	ANIMAL NUMBER	CLINICAL OBSERVATION	BODY AREA
0	2M	8402	SORES	NECK
1	2M	8402	SORES	NECK
	4M	8494	BLOODY CRUST	NOSE
	4M	8495	SORES	NECK
3	1M	8379	BLOODY CRUST	HEAD
	4M	8484	URINE STAINS	ABDOMEN
6	4M	8487	URINE STAINS	INGUINALS-BOTH
			ALOPECIA	ABDOMEN
	4M	8490	URINE STAINS	INGUINALS-BOTH
	4M	8494	SMALL MOVEABLE TISSUE	MASS VENTRL-FT-RGHT
7	4M	8494	SMALL MOVEABLE TISSUE	MASS VENTRL-FT-RGHT
8	1M	8371	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-LEFT
	1M	8372	MALOCCLUSION	
	3M	8453	MALOCCLUSION	
	3M	8455	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8483	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8487	ALOPECIA	INGUINAL-LEFT
	4M	8494	SMALL MOVEABLE TISSUE	MASS VENTRL-FT-RGHT
9	1M	8371	TEETH CUT	
			CHROMODACRYORRHEA	EYE-LEFT
	1M	8372	TEETH CUT	
			CHROMODACRYORRHEA	EYE-RIGHT
	1M	8377	TEETH CUT	
	2M	8420	TEETH CUT	
	3M	8447	TEETH CUT	
			MALOCCLUSION	
			CHROMODACRYORRHEA	EYES-BOTH
	3M	8453	TEETH CUT	
	3M	8455	TEETH CUT	
	4M	8483	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8484	URINE STAINS	SCROTUM
	4M	8494	SMALL MOVEABLE TISSUE	MASS VENTRL-FT-RGHT
10	1M	8371	TEETH CUT	
			CHROMODACRYORRHEA	EYE-LEFT
	2M	8404	TEETH CUT	
	2M	8413	TEETH CUT	
	2M	8415	TEETH CUT	
	2M	8420	MALOCCLUSION	
	3M	8447	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-RIGHT
	3M	8452	TEETH CUT	
	3M	8453	TEETH CUT	
	3M	8455	TEETH CUT	
			CHROMODACRYORRHEA	EYE-RIGHT
	3M	8459	TEETH CUT	
	4M	8483	TEETH CUT	

APPENDIX 2
INDIVIDUAL CLINICAL OBSERVATIONS
2399-108

WEEK	GROUP & SEX	ANIMAL NUMBER	CLINICAL OBSERVATION	BODY AREA
10	4M	8483	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8492	TEETH CUT	
	4M	8494	SORES	AXILLA-RIGHT
11	1M	8371	TEETH CUT	
			CHROMODACRYORRHEA	EYE-LEFT
	1M	8372	TEETH CUT	
	2M	8411	TEETH CUT	
			CHROMODACRYORRHEA	EYE-RIGHT
	2M	8420	TEETH CUT	
	3M	8447	TEETH CUT	
			MALOCCLUSION	
	3M	8455	TEETH CUT	
			CHROMODACRYORRHEA	EYE-RIGHT
	3M	8459	TEETH CUT	
13	4M	8483	TEETH CUT	
			CHROMODACRYORRHEA	EYE-RIGHT
	1M	8367	CHROMODACRYORRHEA	EYE-RIGHT
	1M	8371	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-LEFT
	2M	8411	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-RIGHT
	2M	8420	MALOCCLUSION	
	3M	8447	MALOCCLUSION	
	3M	8455	CHROMODACRYORRHEA	EYES-BOTH
	4M	8483	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8487	BLOODY CRUST	NOSE
			CHROMODACRYORRHEA	EYE-RIGHT

APPENDIX 2
INDIVIDUAL CLINICAL OBSERVATIONS
2399-108

WEEK	GROUP & SEX	ANIMAL NUMBER	CLINICAL OBSERVATION	BODY AREA
2	1F	8400	SORES	NECK
3	1F	8400	SORES	NECK
6	4F	8507	URINE STAINS	INGUINALS-BOTH
	4F	8510	URINE STAINS	INGUINALS-BOTH
	4F	8513	SALIVATION	
	4F	8516	URINE STAINS	INGUINALS-BOTH
	4F	8517	URINE STAINS	INGUINALS-BOTH
7	4F	8510	URINE STAINS	INGUINALS-BOTH
8	1F	8385	SORES	HEAD
	3F	8471	ALOPECIA	LEGS-FORE-BOTH
9	1F	8384	TEETH CUT	
			MALOCCLUSION	
			CHROMODACRYORRHEA	EYES-BOTH
	3F	8476	TEETH CUT	
10	1F	8384	TEETH CUT	
	1F	8394	TEETH CUT	
	2F	8439	TEETH CUT	
	3F	8465	ALOPECIA	LEG-FORE-RIGHT
	3F	8471	ALOPECIA	LEGS-FORE-BOTH
	4F	8516	ALOPECIA	LEGS-FORE-BOTH
	4F	8517	TEETH CUT	
11	1F	8384	TEETH CUT	
	1F	8391	TEETH CUT	
			BLOODY CRUST	NOSE
			CHROMODACRYORRHEA	EYE-LEFT
	3F	8465	ALOPECIA	HEAD
12	1F	8391	BLOODY CRUST	EYE-LEFT
13	1F	8384	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-RIGHT
	4F	8513	SALIVATION	



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- 95 -

APPENDIX 3

Individual Body Weights

APPENDIX 3
INDIVIDUAL BODY WEIGHTS (G)
SUBCHRONIC TOXICITY IN RATS

ANIMAL NUMBER	WEEKS												
	0	1	2	3	4	5	6	7	8	9	10	11	12
GROUP 1 MALES - CONTROL													
8362	235.6	285.7	334.3	371.1	408.4	428.4	461.8	487.7	507.9	525.9	548.8	562.5	582.2
8363	238.5	280.0	316.0	341.1	365.8	384.3	406.1	419.9	433.3	448.8	457.8	459.8	471.5
8364	233.2	287.2	332.4	371.4	407.1	420.5	452.7	472.4	490.6	511.8	535.7	544.9	560.8
8365	243.6	295.9	352.8	401.6	447.8	470.6	501.6	524.5	545.0	571.9	586.6	611.7	632.9
8366	232.3	275.5	311.3	347.0	381.7	382.3	412.4	435.5	447.0	462.4	476.4	476.0	484.8
8367	234.7	283.8	323.5	356.3	394.2	405.0	430.0	451.4	461.4	484.8	488.0	496.3	462.8
8368	236.9	290.7	334.3	374.9	412.0	431.4	451.9	473.2	488.2	504.5	517.9	534.7	547.1
8369	234.3	283.6	327.9	365.7	396.4	416.2	445.7	462.7	469.7	477.1	494.2	516.7	522.8
8370	234.4	284.7	327.3	352.8	382.3	401.6	423.1	436.2	444.7	459.0	468.6	463.8	474.5
8371	242.6	296.9	332.9	373.1	407.9	415.6	441.2	466.5	455.3	468.6	487.6	512.0	519.0
8372	236.0	279.0	317.8	345.7	377.1	394.6	420.1	443.6	456.9	469.8	486.0	492.1	508.7
8373	245.2	301.7	356.7	397.0	441.9	473.1	502.4	516.9	527.5	551.4	575.2	590.8	602.9
8374	224.4	280.0	331.5	369.4	414.2	440.7	460.6	483.8	494.5	513.4	525.0	531.8	541.9
8375	221.6	262.6	303.7	328.1	361.6	378.1	392.6	411.9	423.7	444.2	460.7	474.6	482.9
8376	234.8	287.7	329.6	365.0	408.7	436.5	452.8	467.1	478.2	503.1	519.3	532.8	540.7
8377	222.4	273.9	313.6	345.5	376.7	400.8	420.6	442.5	458.9	473.1	488.8	492.4	504.7
8378	233.3	285.0	328.3	360.0	398.0	419.5	442.5	467.5	476.1	491.7	502.8	513.4	518.1
8379	236.7	291.7	331.2	360.9	388.7	411.1	434.0	453.7	460.9	478.1	486.5	500.7	515.0
8380	244.4	298.3	349.0	381.6	419.5	448.3	470.5	494.1	514.7	533.1	544.5	559.0	570.6
8381	225.8	271.4	317.6	347.1	378.3	403.0	418.6	437.5	449.5	463.5	479.3	489.8	499.5
GROUP 2 MALES - 100.0000 MG/KG													
8402	229.5	259.0	*	*	*	*	*	*	*	*	*	*	*
8403	231.8	287.2	326.5	361.0	393.8	417.8	443.0	466.4	480.8	498.3	507.4	522.0	531.5
8404	234.7	289.9	336.6	369.2	393.3	406.9	435.5	458.6	473.6	491.2	505.5	515.9	528.9
8405	223.2	272.3	306.4	334.0	365.5	375.1	402.8	429.9	435.6	459.5	479.9	502.0	513.5
8406	236.2	291.2	328.8	364.1	400.2	416.8	440.7	455.4	471.4	491.2	502.9	523.8	536.0
8407	223.1	269.8	305.3	338.6	374.0	391.4	417.9	442.9	455.2	461.0	483.5	498.9	504.2
8408	230.4	279.0	325.6	361.3	394.0	403.1	431.0	439.2	448.3	465.0	474.6	486.6	498.7
8409	223.6	268.2	309.0	344.5	377.2	391.0	418.8	431.9	441.7	453.7	470.1	484.4	496.4
8410	239.3	294.9	339.9	378.8	422.0	432.5	460.1	475.8	488.9	501.8	514.2	529.2	544.2
8411	243.6	311.5	375.2	397.4	434.8	454.5	489.0	511.9	526.8	555.1	564.3	587.8	596.5
8412	234.6	286.4	332.7	369.6	411.2	424.6	459.6	479.6	496.8	511.6	525.3	540.7	555.4
8413	219.5	260.5	289.6	330.9	363.0	386.9	408.0	431.5	445.0	463.7	485.9	495.1	508.4
8414	241.5	291.6	339.8	377.2	411.7	435.7	445.8	464.9	486.5	492.4	511.5	528.0	546.9
8415	217.0	261.2	301.3	336.0	358.0	383.0	404.7	402.5	424.0	441.7	453.8	464.9	477.6
8416	235.3	289.4	342.0	389.7	410.7	*	*	*	*	*	*	*	*
8417	233.3	277.8	314.5	*	*	*	*	*	*	*	*	*	*
8418	226.9	275.6	315.8	356.5	395.0	423.6	441.2	463.2	483.7	498.7	514.2	529.0	539.7
8419	234.7	279.4	322.4	359.5	390.2	416.6	431.8	443.3	465.1	479.6	490.8	506.5	513.6
8420	213.7	261.1	301.3	335.0	363.9	386.4	396.1	399.5	415.1	424.0	442.4	457.3	462.3
8421	211.9	251.0	287.3	314.6	339.3	364.6	383.5	383.3	398.4	405.3	423.6	439.2	440.4

* = DEAD ANIMAL

APPENDIX 3 - CONTINUED
INDIVIDUAL BODY WEIGHTS (G)
SUBCHRONIC TOXICITY IN RATS

ANIMAL NUMBER	0	1	2	3	4	5	6	7	8	9	10	11	12	13
GROUP	3	MALES	-	200.0000 MG/KG										
8442	233.9	277.5	317.2	346.5	358.7	366.1	388.8	404.9	419.5	435.7	450.8	462.9	469.7	466.2
8443	218.9	265.8	304.4	333.8	359.0	381.2	398.7	426.8	437.6	457.6	479.3	486.4	500.4	498.0
8444	232.0	283.6	332.4	361.0	386.8	394.7	429.1	444.8	463.5	482.6	498.5	507.2	526.5	518.1
8445	233.7	282.6	322.3	346.9	371.1	380.4	400.7	424.8	432.4	445.7	455.7	469.8	477.3	476.0
8446	233.2	277.3	310.9	337.7	370.3	370.3	409.0	466.8	484.5	470.9	484.5	488.1	493.1	492.7
8447	238.8	288.0	333.7	370.3	370.3	370.3	409.0	466.8	484.5	470.9	484.5	488.1	493.1	492.7
8448	235.5	276.0	307.3	336.1	363.7	363.7	391.8	454.7	400.3	416.8	421.5	439.4	448.8	444.5
8449	203.7	250.0	284.2	313.7	339.6	348.8	371.5	391.8	400.3	416.8	421.5	439.4	448.8	444.5
8450	228.9	275.7	323.0	354.4	386.5	408.6	433.8	454.7	406.5	414.5	440.8	464.6	475.8	468.9
8451	216.5	259.2	292.0	319.1	340.8	347.7	367.5	385.5	406.5	414.5	440.8	464.6	475.8	468.9
8452	234.5	276.4	315.1	340.9	373.9	381.0	396.2	412.7	422.6	430.7	452.8	460.9	454.4	447.9
8453	226.7	271.5	318.7	347.9	379.8	371.4	398.3	411.5	421.7	438.4	455.3	466.5	478.3	458.1
8454	228.5	283.1	325.3	354.9	372.0	397.9	412.3	434.6	440.2	461.0	483.4	461.5	496.0	487.0
8455	213.5	271.9	309.1	334.9	372.0	397.9	412.3	434.6	440.2	461.0	483.4	461.5	496.0	487.0
8456	241.4	290.1	335.6	373.5	400.6	426.6	440.6	457.4	470.3	479.1	487.6	498.6	506.5	515.8
8457	220.8	274.4	320.6	358.0	399.0	422.1	436.6	459.9	474.8	492.2	511.9	528.7	538.5	548.3
8458	207.4	271.9	309.1	334.9	372.0	397.9	412.3	434.6	440.2	461.0	483.4	461.5	496.0	487.0
8459	233.9	279.8	317.9	350.0	383.5	412.4	432.9	445.7	454.0	471.5	481.7	495.5	508.0	517.8
8460	223.3	275.5	316.8	350.6	378.7	404.7	421.3	445.7	459.6	470.7	483.0	495.9	511.1	518.6
8461	232.8	281.3	326.7	357.2	380.6	412.2	431.6	441.8	458.4	474.8	486.8	499.8	513.5	524.0
GROUP	4	MALES	-	800.0000 MG/KG										
8482	240.4	278.1	325.3	342.0	365.8	397.1	421.6	436.1	452.5	458.4	472.3	484.9	500.2	490.5
8483	246.4	298.8	337.2	356.7	372.8	396.0	421.6	436.1	452.5	458.4	472.3	484.9	500.2	490.5
8484	228.2	272.3	284.1	300.8	343.7	367.4	387.7	397.0	388.5	398.0	417.2	428.3	443.0	438.4
8485	222.5	254.6	266.7	293.9	320.5	328.9	344.7	345.3	362.6	360.3	376.8	380.7	389.0	386.8
8486	219.7	268.6	293.5	322.3	354.5	366.5	384.9	407.4	424.9	428.7	446.2	464.1	479.2	474.0
8487	236.0	285.1	317.5	349.2	379.8	373.3	394.4	404.1	413.0	415.6	438.3	455.0	463.2	447.9
8488	225.8	268.0	288.9	320.1	342.5	346.7	379.3	398.0	381.2	390.7	401.1	413.1	382.1	401.5
8489	217.2	243.3	278.8	252.0	300.6	313.3	349.1	358.6	371.0	366.1	388.8	397.5	405.2	395.1
8490	217.5	252.2	289.4	308.4	334.7	343.8	367.0	375.0	385.8	397.2	411.5	420.1	428.4	426.2
8491	231.8	262.7	296.6	312.4	342.4	344.6	369.5	349.6	371.0	366.1	388.8	397.5	405.2	395.1
8492	237.1	284.7	312.8	335.1	371.8	392.3	412.0	400.3	410.5	422.9	444.4	451.2	463.2	460.0
8493	228.6	278.0	311.5	335.1	371.8	392.3	412.0	400.3	410.5	422.9	444.4	451.2	463.2	460.0
8494	227.5	233.2	264.7	281.1	320.4	351.6	386.0	384.1	390.9	402.2	408.1	427.1	441.0	444.7
8495	216.1	231.2	264.1	299.6	334.1	354.7	369.7	370.5	383.1	389.8	402.8	420.3	425.9	424.3
8496	234.0	282.1	295.8	327.7	363.9	400.7	414.7	430.7	444.8	454.6	453.7	467.3	476.2	471.3
8497	243.3	254.2	297.6	334.4	366.3	390.4	416.5	422.0	433.3	441.5	443.1	456.9	466.5	469.8
8498	225.7	277.3	310.7	329.4	365.7	397.6	401.9	421.9	431.6	435.6	443.1	451.6	470.8	474.4
8499	227.2	253.3	290.5	324.9	364.5	392.6	415.9	421.8	431.6	435.6	443.1	451.6	470.8	474.4
8500	219.0	263.1	292.4	323.3	354.5	373.3	404.2	407.6	426.4	429.8	453.1	454.6	460.8	468.3
8501	232.4	260.7	290.7	309.9	346.8	364.0	377.9	382.3	392.8	395.3	416.8	436.3	425.7	461.0

* = DEAD ANIMAL

APPENDIX 3 - CONTINUED
INDIVIDUAL BODY WEIGHTS (G)
SUBCHRONIC TOXICITY IN RATS

PAGE 98

HLA 2399108

ANIMAL NUMBER	0	1	2	3	4	5	6	7	8	9	10	11	12	13
GROUP	1 FEMALES - CONTROL													
8382	159.3	180.3	199.0	218.3	236.8	242.0	255.6	266.1	271.5	277.4	279.6	289.6	294.3	290.3
8383	157.3	171.6	190.0	205.2	218.9	207.6	231.6	235.9	236.6	249.4	259.9	257.1	257.2	261.5
8384	164.6	185.8	200.2	219.0	238.9	245.7	270.5	287.1	294.7	281.3	299.2	310.3	320.3	310.4
8385	161.7	186.6	205.0	213.0	216.8	236.1	247.6	249.3	250.3	263.1	269.3	272.1	278.2	268.1
8386	155.3	173.3	186.9	194.0	210.5	221.3	227.3	233.9	241.4	242.6	248.3	261.9	264.9	256.7
8387	164.4	180.6	199.7	215.1	226.3	234.1	239.6	253.8	257.2	262.3	271.2	268.3	278.8	269.3
8388	165.1	181.3	204.8	206.0	221.5	221.4	235.3	238.9	248.4	248.6	259.7	262.6	265.3	265.4
8389	165.6	190.2	210.8	223.8	225.2	255.8	254.9	284.9	270.2	279.8	286.0	277.2	296.0	286.0
8390	155.9	178.8	196.9	216.6	225.8	243.0	252.0	253.5	260.2	266.4	276.8	269.5	281.4	276.7
8391	169.3	191.7	213.8	229.9	246.1	244.1	273.7	291.3	294.2	303.7	310.3	312.9	301.7	299.9
8392	162.7	202.0	206.8	234.1	249.7	264.5	293.5	263.7	290.4	298.1	325.3	307.4	303.4	309.6
8393	158.9	187.1	205.1	211.0	229.1	238.4	243.0	247.4	256.6	260.7	267.6	277.2	276.1	280.7
8394	160.1	182.6	195.7	206.5	210.0	226.3	233.2	234.2	232.4	235.4	239.9	254.0	254.1	255.8
8395	163.8	181.7	205.0	217.3	224.1	238.8	240.2	251.8	228.3	276.5	270.6	272.7	275.4	281.3
8396	163.7	177.0	194.7	210.5	227.7	229.2	238.3	246.7	250.3	258.1	260.3	262.5	263.8	262.8
8397	154.0	176.9	197.5	216.4	230.7	236.8	254.0	253.3	263.4	268.5	271.7	275.8	286.6	290.8
8398	158.6	176.1	192.6	204.1	208.5	217.0	216.9	219.7	221.2	234.2	237.7	235.1	233.9	239.0
8399	170.5	197.8	225.2	244.5	256.7	275.0	280.4	289.2	285.3	295.6	303.6	301.6	307.4	307.8
8400	155.4	179.2	195.7	206.2	219.1	229.3	238.5	240.2	252.3	266.5	261.9	260.1	268.4	261.0
8401	173.4	187.0	210.1	223.1	236.0	244.6	256.4	256.9	262.5	271.5	271.9	267.6	276.6	284.8
GROUP	2 FEMALES - 100.0000 MG/KG													
8422	156.9	182.1	203.7	215.8	234.2	241.6	243.5	251.4	259.8	263.4	271.5	271.2	276.2	278.3
8423	154.9	173.5	192.7	213.6	223.8	228.5	245.5	254.2	252.3	250.0	262.4	269.5	271.1	269.8
8424	163.2	182.5	201.0	218.8	219.8	237.3	238.4	257.6	262.6	262.8	271.2	279.8	291.8	284.1
8425	163.6	184.1	203.3	217.5	229.7	228.6	249.5	255.5	258.6	262.9	270.3	276.0	274.3	280.2
8426	142.9	178.9	187.0	206.5	215.6	221.6	236.6	242.9	246.3	243.6	249.8	258.2	254.6	250.3
8427	164.4	187.3	217.5	225.3	246.4	234.1	257.4	269.0	272.2	282.3	280.3	279.8	290.7	287.9
8428	164.0	184.5	196.6	211.6	237.2	233.7	233.7	256.5	267.5	268.1	269.0	279.8	293.8	289.0
8429	161.2	190.7	212.5	230.6	238.3	256.8	257.2	277.7	268.9	294.5	291.5	297.7	296.0	302.9
8430	156.3	175.0	193.0	205.6	210.3	212.9	218.2	229.6	237.2	241.9	245.4	245.0	238.1	242.4
8431	165.1	192.9	205.1	226.0	237.2	232.0	249.3	255.3	258.4	260.3	269.2	277.0	272.1	265.7
8432	165.2	178.7	195.5	201.6	222.0	234.1	242.3	239.4	251.1	257.4	257.2	273.4	266.6	266.1
8433	163.5	182.0	201.9	216.9	223.0	244.5	245.8	251.9	262.5	262.1	270.6	272.3	279.1	280.6
8434	157.3	171.5	186.5	201.3	211.1	219.5	222.0	231.8	238.2	250.1	244.2	255.3	259.0	254.7
8435	162.0	180.4	195.3	207.0	223.4	233.5	237.5	238.4	234.9	254.0	257.1	256.8	257.3	263.7
8436	169.2	188.6	195.1	222.6	225.5	246.8	257.5	255.8	255.0	267.9	267.2	263.4	274.4	280.0
8437	157.1	172.0	187.6	194.2	213.1	225.3	232.1	228.6	238.3	252.5	245.5	241.6	252.3	257.5
8438	154.2	182.2	196.0	222.0	233.3	250.2	260.1	256.4	266.2	264.9	273.6	282.5	299.7	295.7
8439	167.5	186.5	206.2	222.8	235.2	247.7	249.7	260.6	267.8	270.3	271.9	268.6	273.8	279.7
8440	153.1	186.2	201.5	202.9	217.6	229.1	237.6	235.6	247.0	258.4	257.5	252.6	265.8	272.6
8441	167.1	194.0	206.7	225.7	236.5	249.3	247.2	259.6	262.7	267.4	272.0	270.1	276.6	272.0

APPENDIX 3 - CONTINUED
INDIVIDUAL BODY WEIGHTS (G)
SUBCHRONIC TOXICITY IN RATS

ANIMAL NUMBER	GROUP	WEEKS												
		0	1	2	3	4	5	6	7	8	9	10	11	12
	3 FEMALES - 200.0000 MG/KG													
8462	164.6	186.9	198.5	215.7	233.7	237.7	243.2	254.1	256.5	257.0	260.8	267.4	263.3	
8463	152.8	173.6	178.5	198.1	221.0	225.6	227.3	237.2	246.0	244.7	243.7	247.7	246.8	
8464	152.8	168.1	191.8	205.3	220.3	231.6	237.9	242.4	245.9	254.6	254.6	261.2	250.6	
8465	166.1	177.1	191.3	207.2	218.8	227.7	221.7	240.7	252.6	247.1	255.7	257.1	255.6	
8466	163.0	178.2	207.8	220.4	238.7	244.4	255.6	266.2	277.7	282.0	284.5	288.6	*	
8467	153.5	181.4	198.4	215.5	212.3	226.6	247.1	247.5	262.5	271.6	263.6	264.6	268.0	
8468	158.2	178.2	190.5	*	*	*	*	*	*	*	*	*	*	
8469	174.8	181.0	215.1	226.1	242.3	244.9	261.5	259.3	269.3	271.5	269.8	267.8	272.0	
8470	154.7	167.2	190.2	199.3	215.2	218.5	229.4	235.1	241.1	247.2	251.9	254.3	250.7	
8471	157.9	174.0	195.8	213.0	230.5	228.5	245.7	256.8	260.1	268.4	271.3	270.6	263.7	
8472	162.9	183.8	204.3	219.7	225.9	240.4	255.5	275.8	272.6	286.2	304.2	304.6	302.9	
8473	156.2	169.5	*	*	*	*	*	*	*	*	*	*	*	
8474	160.1	174.5	201.9	211.9	204.0	228.1	229.4	252.7	248.6	260.5	266.9	263.7	264.1	
8475	162.2	187.9	207.0	218.1	231.2	237.6	249.4	251.8	255.6	260.7	272.1	266.9	288.0	
8476	165.8	185.9	207.9	224.5	240.0	246.2	255.2	258.9	270.5	269.1	272.5	275.8	277.7	
8477	164.7	180.4	211.2	233.6	253.3	260.7	255.5	267.4	274.1	277.7	285.4	295.1	296.2	
8478	157.9	173.1	*	*	*	*	*	*	*	*	*	*	*	
8479	151.7	167.0	185.4	194.7	198.8	208.0	218.7	219.6	235.7	227.8	233.1	232.2	238.5	
8480	158.3	165.5	192.0	204.0	229.5	228.6	249.2	256.1	255.5	266.8	269.1	272.2	269.6	
8481	155.7	175.3	196.4	211.8	222.5	235.3	244.8	253.3	251.1	263.9	273.2	270.6	274.8	
	4 FEMALES - 800.0000 MG/KG													
8502	153.8	175.5	193.5	216.2	224.8	233.5	242.4	248.6	258.9	269.9	265.7	268.9	283.6	
8503	156.2	175.2	189.7	207.1	220.8	224.3	237.4	240.3	244.2	252.2	254.2	253.1	250.1	
8504	156.2	166.3	186.4	193.0	214.4	220.9	233.2	236.5	237.2	241.3	257.5	248.4	245.2	
8505	156.1	165.5	*	*	*	*	*	*	*	*	*	*	*	
8506	167.5	185.2	199.1	203.2	220.5	225.4	230.0	224.9	236.8	246.1	243.8	254.6	253.2	
8507	168.9	187.1	211.2	227.2	243.6	252.4	260.0	254.4	269.9	273.1	283.5	286.5	287.1	
8508	156.3	176.5	198.1	207.8	221.2	227.4	233.7	234.5	232.1	244.4	254.9	252.3	251.7	
8509	163.4	166.8	191.9	208.3	218.7	214.7	223.5	219.6	223.5	228.0	239.4	242.7	237.1	
8510	153.8	169.8	176.5	181.8	198.8	204.8	196.7	213.1	218.4	226.6	237.3	233.2	222.8	
8511	156.4	170.1	192.9	208.1	217.2	230.8	233.1	244.3	249.9	250.5	257.3	261.9	256.5	
8512	172.8	184.5	214.4	235.1	237.2	253.8	259.2	271.5	269.2	271.5	279.6	288.1	278.0	
8513	151.3	165.7	185.5	202.8	207.1	222.8	232.6	232.7	236.9	242.5	249.5	249.3	252.9	
8514	161.1	166.6	191.3	197.7	211.6	227.5	236.2	235.9	248.3	251.4	265.1	*	*	
8515	166.8	171.9	*	*	*	*	*	*	*	*	*	*	*	
8516	162.1	171.3	205.0	220.7	233.1	239.8	246.5	254.8	248.7	266.4	237.1	268.0	282.1	
8517	154.6	166.5	175.8	200.1	198.1	213.5	217.8	225.5	219.7	239.1	253.0	232.8	239.0	
8518	155.2	176.2	191.5	200.5	218.1	217.9	224.0	232.4	242.2	239.9	245.2	255.0	259.4	
8519	172.0	197.9	210.9	225.9	223.7	248.3	251.9	258.2	255.7	257.3	259.7	267.5	267.0	
8520	142.1	160.2	173.4	180.5	195.3	203.2	207.2	207.2	207.2	207.2	207.2	207.2	207.2	
8521	166.3	181.8	203.9	212.9	227.1	237.5	248.5	248.5	250.1	251.7	258.1	262.2	271.2	

* = DEAD ANIMAL



HAZLETON

LABORATORIES AMERICA, INC.

1330 - B PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

HLA 2399-108

- 100 -

APPENDIX 4

Individual Food Consumption

APPENDIX 4
INDIVIDUAL FOOD CONSUMPTION (G/WK)
SUBCHRONIC TOXICITY IN RATS

ANIMAL NUMBER	WEEKS												
	1	2	3	4	5	6	7	8	9	10	11	12	13
GROUP 1 MALES - CONTROL													
8362	161.6	178.1	171.0	165.2	**	183.2	175.9	175.5	176.0	177.7	173.1	181.4	**
8363	174.2	165.9	157.4	137.0	**	158.0	147.8	150.8	150.5	145.3	140.0	143.1	**
8364	207.3	184.0	181.8	170.6	**	180.0	167.1	172.5	168.6	179.7	172.3	170.9	**
8365	183.8	186.7	195.7	191.4	**	193.8	192.9	182.5	199.5	190.8	192.6	189.7	**
8366	169.9	170.1	170.3	166.4	**	164.2	156.4	162.3	164.4	166.5	148.4	152.5	**
8367	154.8	185.4	191.9	206.4	**	162.2	166.9	170.0	168.9	155.7	161.1	116.7	**
8368	207.7	185.9	192.6	172.5	**	170.7	168.0	160.7	169.0	165.1	160.0	152.3	**
8369	174.7	173.0	169.1	149.5	**	167.9	163.2	150.0	174.1	154.9	154.1	151.4	**
8370	164.1	167.0	158.0	151.5	**	155.2	147.4	144.9	141.8	145.8	135.2	130.2	**
8371	185.4	173.8	176.9	176.0	**	191.1	184.4	140.9	155.8	160.5	154.2	152.9	**
8372	165.7	168.5	159.3	152.2	142.9	153.1	150.6	159.3	155.6	158.5	154.2	152.9	140.7
8373	194.6	197.6	190.6	195.9	182.7	197.9	177.2	179.4	187.1	191.4	193.9	185.7	175.0
8374	185.6	196.0	189.2	193.5	180.1	180.0	178.9	173.8	177.0	177.0	169.0	161.9	161.3
8375	164.0	165.7	159.8	154.6	141.0	151.3	152.8	155.3	158.4	159.6	157.7	144.4	146.2
8376	178.4	173.0	174.3	184.5	181.0	175.9	168.0	169.3	176.6	169.8	174.5	163.9	158.6
8377	174.9	165.0	169.6	163.8	161.2	174.3	163.9	172.5	174.7	176.3	**	168.9	176.2
8378	162.1	171.6	166.3	169.6	154.4	164.4	158.1	152.1	154.4	155.6	157.6	144.3	142.2
8379	178.9	171.3	163.9	151.9	152.7	164.1	170.8	151.6	172.9	151.6	153.2	151.3	147.2
8380	189.3	192.5	190.4	183.9	174.7	183.3	179.4	182.0	179.6	174.8	176.8	167.2	175.2
8381	162.6	168.8	167.4	163.8	158.8	158.3	146.4	149.7	151.9	149.9	152.8	147.3	155.6
GROUP 2 MALES - 100.0000 MG/KG													
8402	145.0	179.4	175.8	162.7	**	170.0	173.7	159.4	161.8	159.7	159.8	153.6	**
8403	177.3	183.8	182.3	160.4	**	166.5	171.9	168.8	164.8	163.1	156.9	165.8	**
8404	181.5	176.2	173.3	166.8	**	169.5	170.1	156.0	187.2	158.9	171.2	171.8	**
8405	190.4	188.1	190.2	179.7	**	185.0	170.8	175.5	174.3	171.6	173.3	172.5	**
8406	165.5	160.6	161.5	159.9	**	162.8	**	149.8	142.5	149.2	148.6	143.7	**
8407	166.2	173.4	168.7	199.6	**	154.3	145.8	146.7	151.6	147.1	147.3	147.0	**
8408	168.7	170.7	166.3	163.3	**	165.8	155.0	148.1	152.9	157.5	152.4	156.4	**
8409	180.1	183.4	175.0	179.9	**	173.1	169.4	157.0	161.2	156.3	167.1	168.3	**
8410	210.7	200.8	193.5	189.5	**	196.2	192.6	181.6	**	178.5	168.0	162.3	**
8412	176.0	181.4	180.9	176.7	**	178.6	164.8	163.1	160.2	161.9	164.6	164.3	158.9
8413	164.3	156.0	164.6	167.1	**	155.3	157.4	151.4	160.5	167.7	168.4	164.3	155.2
8414	192.2	185.0	179.8	175.4	163.7	160.8	164.9	164.5	158.3	161.0	162.7	168.0	163.9
8415	169.0	**	171.8	167.4	156.9	161.2	148.1	**	171.6	159.9	**	163.2	**
8416	201.5	211.2	**	200.7	**	**	**	**	**	**	**	**	**
8417	165.8	163.3	**	**	**	**	**	**	**	**	**	**	**
8418	168.0	184.5	170.2	175.1	173.0	172.9	167.3	165.6	161.5	160.2	160.1	157.0	150.7
8419	172.7	168.0	173.6	165.6	161.5	154.3	152.6	157.0	161.3	159.3	150.2	149.0	140.2
8420	160.4	161.8	158.6	151.9	149.7	139.6	127.5	144.7	139.7	152.7	143.9	152.7	132.6
8421	170.6	159.3	157.4	152.5	148.1	150.8	138.0	144.4	145.0	135.6	141.6	146.0	135.7

* = DEAD ANIMAL
** = INVALID VALUE - FOOD WASTED OR SPILLED

ANIMAL NUMBER	GROUP	WEEKS												
		1	2	3	4	5	6	7	8	9	10	11	12	13
	3 MALES	200.0000 MG/KG												
8442		193.9	167.9	158.5	138.3	**	143.7	141.3	144.9	140.7	149.1	146.2	141.6	**
8443		163.9	172.2	180.1	146.6	**	158.3	156.0	152.2	149.3	158.9	**	153.5	**
8444		172.6	177.5	176.2	164.7	**	155.5	149.2	154.9	159.2	163.7	155.8	151.1	**
8445		184.9	181.4	168.1	152.2	**	161.4	163.1	155.4	157.7	150.9	**	156.8	**
8446		181.2	187.3	**	*	*	*	*	*	*	*	*	*	*
8447		168.9	172.1	172.6	170.8	**	176.1	163.4	160.9	129.5	140.1	132.9	123.6	**
8448		172.6	162.0	156.3	154.8	*	*	*	*	*	*	*	*	*
8449		151.1	157.5	154.6	141.1	**	137.8	142.3	133.1	136.3	143.6	138.4	138.8	**
8450		177.1	182.3	172.9	159.7	**	171.0	159.7	*	*	*	*	*	*
8451		161.1	157.8	157.8	156.5	**	151.1	155.2	154.7	152.6	162.6	157.6	175.3	**
8452		164.3	162.8	161.5	158.8	**	147.5	146.6	127.9	136.1	151.6	137.3	125.3	**
8453		185.9	198.3	194.8	186.1	**	162.1	**	147.1	162.6	180.4	**	165.3	**
8454		190.5	192.5	*	*	*	*	*	*	*	*	*	*	*
8455		160.6	168.6	161.7	157.7	158.6	147.8	155.2	143.6	155.1	157.4	95.8	164.9	**
8456		178.8	172.8	174.7	167.5	166.3	161.8	158.5	153.5	150.3	151.3	144.6	142.6	144.2
8457		173.9	182.2	176.8	175.0	163.0	156.8	158.7	161.7	156.5	158.6	163.8	159.7	149.0
8458		*	*	*	*	*	*	*	*	*	*	*	*	*
8459		174.1	176.0	163.9	198.9	164.5	164.7	150.7	154.4	157.4	166.2	149.5	159.9	156.7
8460		170.0	177.0	171.5	160.6	157.4	167.4	163.9	162.2	151.3	153.8	**	153.1	189.1
8461		173.6	174.2	173.5	156.1	167.3	162.6	158.3	161.6	155.7	156.7	152.2	152.2	151.3
	4 MALES	800.0000 MG/KG												
8482		159.1	172.1	163.9	181.9	**	180.6	165.2	167.0	167.6	**	176.1	170.1	**
8483		194.3	189.0	165.3	160.0	**	175.7	147.6	147.9	158.4	147.6	181.2	174.7	**
8484		169.7	145.1	109.1	186.0	**	157.7	160.3	152.1	150.9	154.8	161.1	159.8	**
8485		160.6	137.1	137.8	143.7	**	149.9	141.9	142.2	139.7	130.3	145.8	124.9	**
8486		176.9	151.9	183.1	193.6	**	190.1	**	**	154.1	177.4	181.4	175.8	**
8487		180.0	166.1	171.8	183.5	**	151.5	**	149.3	153.5	155.5	173.7	163.0	**
8488		152.8	138.8	149.5	139.7	**	150.6	158.6	96.7	164.4	143.6	139.0	96.7	**
8489		157.8	159.5	112.0	141.4	**	151.7	158.3	150.3	150.7	135.9	133.5	141.1	**
8490		154.2	160.7	148.5	146.6	**	153.6	142.6	143.5	151.6	149.6	150.6	153.4	**
8491		157.3	162.3	153.8	162.1	**	166.5	121.8	*	*	*	*	*	*
8492		171.8	167.9	166.9	162.1	160.5	151.5	134.7	138.4	151.2	157.5	151.2	155.0	*
8493		169.5	161.5	*	*	*	*	*	*	*	*	*	*	*
8494		138.8	67.8	164.7	148.9	148.1	165.3	141.9	146.5	143.5	143.8	143.4	149.6	133.0
8495		117.4	139.3	147.6	144.6	150.3	132.4	119.4	128.9	124.1	138.4	142.9	144.3	127.3
8496		178.0	161.0	165.8	**	197.4	180.0	171.8	178.3	206.2	**	218.1	183.9	153.5
8497		161.0	143.4	177.5	171.4	169.1	167.0	160.6	**	172.8	**	163.9	188.8	178.2
8498		172.5	164.8	161.5	167.7	146.0	155.9	**	**	156.0	**	170.8	171.3	151.2
8499		140.4	162.8	164.8	166.6	157.8	161.7	161.2	168.4	139.2	145.5	152.2	156.5	123.4
8500		165.1	161.4	158.3	160.3	156.9	162.9	160.8	161.9	166.3	162.0	161.6	146.8	148.1
8501		148.0	154.3	155.7	159.6	144.8	148.0	150.1	151.8	144.0	150.2	155.4	156.1	153.7

* = DEAD ANIMAL
** = INVALID VALUE - FOOD WASTED OR SPILLED

APPENDIX 4 - CONTINUED
INDIVIDUAL FOOD CONSUMPTION (G/WK)
SUBCHRONIC TOXICITY IN RATS

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13
GROUP	1 FEMALES - CONTROL												
8382	115.8	151.6	**	114.1	**	125.7	118.6	111.0	117.7	118.7	**	109.6	**
8383	119.9	126.2	129.6	122.1	**	**	119.0	**	126.0	133.4	114.5	111.2	**
8384	133.2	136.2	147.5	142.1	**	152.8	158.0	142.4	**	**	**	129.1	**
8385	143.8	145.6	129.8	121.2	**	133.4	132.4	126.6	155.6	133.6	**	123.2	**
8386	129.0	122.0	119.4	123.8	**	141.8	131.2	114.4	129.3	127.3	134.0	109.5	**
8387	129.1	119.3	138.4	116.5	**	124.4	137.1	124.5	122.6	130.4	114.6	119.6	**
8388	138.9	143.8	137.4	118.5	**	123.9	126.1	119.2	135.3	119.7	**	112.1	**
8389	147.5	153.5	147.5	151.0	**	148.4	150.1	133.0	152.8	141.4	116.4	135.4	**
8390	129.1	131.6	141.8	119.1	**	129.2	126.9	125.1	124.7	127.7	110.6	118.0	**
8391	134.1	141.5	132.3	129.9	**	146.5	140.8	135.3	141.7	127.0	135.6	87.7	**
8392	156.1	153.2	147.9	154.1	**	169.7	121.9	142.5	143.1	165.7	126.8	116.8	125.3
8393	126.3	131.4	128.7	122.5	143.1	116.0	122.9	121.0	127.5	126.4	117.6	113.9	126.8
8394	125.6	120.7	117.6	104.4	124.8	118.6	110.1	110.6	82.3	130.0	113.3	112.2	110.7
8395	126.4	125.0	123.2	106.5	112.6	122.2	121.0	76.2	149.2	129.1	103.3	113.6	125.4
8396	125.8	128.4	127.9	119.6	111.6	130.0	120.1	**	117.5	116.2	111.9	110.3	107.3
8397	123.6	128.2	**	**	140.7	129.4	**	109.5	99.8	105.9	107.3	109.1	111.9
8398	126.6	136.3	121.4	108.1	109.8	113.5	111.4	**	129.4	118.5	117.1	133.2	105.8
8399	135.4	141.7	144.2	128.7	128.2	127.4	126.3	**	123.9	126.5	107.6	123.5	121.5
8400	110.9	101.5	**	**	102.9	112.2	104.4	**	110.7	**	**	108.9	97.5
8401	128.3	132.5	127.8	119.2	117.7	131.6	125.1	119.9	111.5	118.6	111.8	117.3	113.0
GROUP	2 FEMALES - 100.0000 MG/KG												
8422	124.1	120.6	123.0	121.4	**	116.1	115.7	113.9	110.9	113.5	108.6	106.7	**
8423	143.8	**	146.2	126.2	**	129.4	123.5	125.8	119.9	118.2	125.6	119.4	**
8424	132.8	131.0	147.9	137.0	**	167.3	145.2	135.2	143.0	129.2	134.0	137.4	**
8425	**	111.6	**	124.6	**	140.1	130.2	126.6	130.0	131.8	126.6	114.3	**
8426	144.8	133.7	148.3	119.2	**	132.4	126.0	116.4	112.0	112.5	116.5	107.0	**
8427	141.5	153.6	143.7	137.8	**	135.3	131.6	130.5	135.2	119.3	123.3	116.1	**
8428	138.6	136.9	153.6	138.4	**	154.1	150.0	144.6	128.8	127.7	135.4	137.6	**
8429	158.5	156.5	152.7	139.8	**	119.8	129.2	189.8	147.7	131.7	129.9	139.8	**
8430	137.7	128.1	**	107.1	**	127.8	117.5	120.1	116.2	124.0	111.2	99.1	**
8431	133.9	126.2	132.1	121.7	**	120.8	109.9	103.2	111.4	115.2	111.3	92.5	**
8432	171.6	127.4	**	125.0	136.0	127.3	126.7	**	**	136.1	**	**	**
8433	119.2	132.8	133.9	119.1	118.5	118.1	111.0	179.3	114.9	115.2	111.7	111.3	112.4
8434	117.3	122.7	127.9	104.8	105.1	106.1	108.8	110.7	111.1	102.9	106.9	102.3	99.7
8435	122.9	124.1	127.3	114.8	118.9	123.4	115.3	121.3	158.0	127.5	130.0	122.5	122.5
8436	146.5	151.7	160.5	153.0	153.9	**	125.7	134.7	143.3	130.0	**	134.7	132.3
8437	119.1	133.5	127.5	117.0	114.4	122.9	119.7	119.7	106.9	111.1	107.2	110.3	105.3
8438	127.6	129.8	136.2	125.0	115.2	122.9	107.8	106.4	108.8	107.4	109.2	118.1	103.9
8439	148.2	138.4	141.2	127.7	137.4	136.4	127.0	129.5	129.2	130.6	102.4	139.2	124.4
8440	149.6	130.1	120.4	132.0	126.4	147.2	**	130.5	138.5	137.5	136.3	136.8	131.6
8441	145.9	133.1	143.9	130.9	125.1	122.7	127.6	121.9	121.5	124.3	119.9	110.0	202.4

** - INVALID VALUE - FOOD WASTED OR SPILLED

APPENDIX 4 - CONTINUED
INDIVIDUAL FOOD CONSUMPTION (G/WK)
SUBCHRONIC TOXICITY IN RATS

ANIMAL NUMBER	GROUP	WEEKS												
		1	2	3	4	5	6	7	8	9	10	11	12	13
	3 FEMALES - 200.0000 MG/KG													
8462		154.2	145.3	147.7	133.3	**	140.4	128.3	125.8	125.2	115.1	118.4	113.0	**
8463		116.6	96.4	122.0	103.9	**	99.5	101.2	101.2	98.6	99.7	96.8	96.2	**
8464		124.8	139.1	132.3	129.0	**	124.4	120.9	109.7	124.7	126.7	115.6	114.7	**
8465		145.8	164.9	166.1	**	**	**	**	177.7	**	**	**	187.9	**
8466		137.7	145.9	143.4	145.6	**	135.6	133.4	139.5	147.8	134.7	131.9	134.2	**
8467		150.7	135.7	138.9	125.5	**	127.7	**	128.9	145.3	**	105.7	118.3	**
8468		127.7	119.2	*	*	*	*	*	*	*	*	*	*	*
8469		138.9	142.8	136.8	132.1	**	120.7	120.2	99.1	121.8	125.4	93.2	115.4	**
8470		117.2	128.8	114.5	117.9	**	109.7	104.2	104.4	107.4	110.3	103.8	107.4	**
8471		141.2	143.1	155.2	146.9	**	141.9	137.5	130.8	142.2	130.1	129.1	123.8	**
8472		134.7	131.0	133.6	116.7	**	133.6	135.6	122.3	162.5	120.0	119.7	123.8	**
8473		121.3	*	*	*	*	*	*	*	*	*	*	*	*
8474		112.8	124.4	**	108.0	118.5	146.9	130.5	131.0	127.1	134.2	114.3	113.6	120.4
8475		130.6	131.4	133.7	123.1	123.2	128.3	125.7	127.8	130.5	129.8	126.9	127.5	**
8476		132.5	132.6	133.9	120.0	131.9	133.6	112.5	116.5	119.0	118.6	124.8	117.7	118.7
8477		139.9	146.1	154.5	142.9	130.6	118.6	119.7	121.5	106.7	113.7	102.5	115.8	104.6
8478		117.3	*	*	*	*	*	*	*	*	*	*	*	*
8479		**	149.8	**	102.3	96.2	109.1	107.1	102.0	101.4	100.4	99.5	98.2	98.9
8480		175.1	148.5	141.8	134.6	125.7	145.1	120.2	127.2	137.2	136.1	120.3	114.6	130.1
8481		131.0	137.5	135.1	128.2	130.3	125.2	127.6	122.9	129.9	124.2	123.1	126.0	123.2
	4 FEMALES - 800.0000 MG/KG													
8502		142.6	131.2	151.3	155.5	**	164.8	**	148.3	129.9	**	**	173.8	**
8503		129.8	120.9	132.1	134.5	**	126.6	107.3	106.8	110.4	**	112.9	104.6	**
8504		120.1	117.5	**	120.7	**	125.3	108.6	**	**	**	**	108.5	**
8505		108.5	*	*	*	*	*	*	*	*	*	*	*	*
8506		137.9	135.3	139.4	135.5	**	117.7	115.3	137.3	125.8	123.3	**	141.6	**
8507		148.5	149.1	155.7	152.2	**	135.1	110.2	130.3	134.7	133.5	145.6	130.4	**
8508		119.6	128.1	122.2	**	**	93.4	120.9	108.3	**	102.8	119.8	105.2	**
8509		130.1	126.7	128.1	113.4	**	101.7	122.9	107.1	111.7	117.4	116.3	119.3	**
8510		113.0	103.9	112.7	**	**	89.6	125.9	97.3	117.3	108.2	111.9	103.9	**
8511		126.1	141.8	128.4	128.9	**	117.1	119.6	124.9	107.7	101.0	122.3	109.6	**
8512		119.6	131.3	148.7	**	**	158.9	**	**	135.8	148.8	186.4	128.6	**
8513		134.1	142.0	148.0	135.5	141.5	129.8	133.9	132.8	128.3	113.5	124.2	119.1	116.9
8514		115.9	135.6	136.1	137.9	177.4	163.3	**	136.6	138.8	138.2	180.1	*	*
8515		135.2	*	*	*	*	*	*	*	*	*	*	*	*
8516		134.3	187.0	**	**	**	165.8	**	**	134.6	132.2	131.2	141.5	165.8
8517		129.7	124.0	140.3	131.8	135.2	**	**	134.6	128.6	121.2	123.6	126.4	121.6
8518		130.3	121.7	124.4	116.2	115.8	103.4	125.1	123.1	169.3	114.1	113.4	124.6	115.9
8519		139.9	140.1	**	129.9	137.3	121.4	116.0	112.0	114.8	105.2	114.8	111.1	114.0
8520		116.1	109.6	134.5	127.2	123.1	107.0	*	*	*	*	*	*	*
8521		125.1	136.4	128.3	**	135.8	121.2	129.0	121.3	115.7	120.9	114.7	121.6	125.6

* = DEAD ANIMAL
** = INVALID VALUE - FOOD WASTED OR SPILLED



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- 105 -

APPENDIX 5

Individual Ophthalmoscopic Findings



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APPENDIX 5

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS

<u>Animal Number</u>	<u>Group</u>	<u>Sex</u>	<u>Interval</u>	<u>Finding</u>
8404	2	M	Pretest	Left eye - Small hyaloid remnants with small vitreal hemorrhages (judged by ophthalmologist to be a common developmental finding which would not affect test results).
8418	2	M	Pretest	Left eye - Small hyaloid remnants with small vitreal hemorrhages (judged by ophthalmologist to be a common developmental finding which would not affect test results).
8373	1	M	Terminal	Right eye - focal zone of retinal degeneration
8452	3	M	Terminal	Right eye - generalized retinal degeneration. Left eye - early diffuse retinal degeneration.



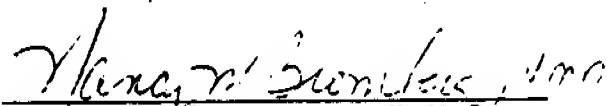
Nancy M. Bromberg, V.M.D., M.S.
Diplomate, American College of Veterinary Ophthalmologists
4105 Brandywine Street, Northwest
Washington, D.C. 20016
202/363-7303

April 1, 1986

Gary W. Wolfe, Ph.D.
1330 -B Piccard Drive
Rockville, MD 20850

Subject: Ophthalmoscopic Examination of 240 Rats, Study 2399-108
March 27, 1986

All animals were found to have no visible lesions except the following;
male # 86 and male # 110 - both had small hyaloid remenants with small vitreal hemorrhages in their left eyes. This is a commonly identified developmental abnormality. Its presence will not affect test outcome.


Nancy M. Bromberg, V.M.D.



Nancy M. Bromberg, V.M.D., M.S.
Diplomate, American College of Veterinary Ophthalmologists
4105 Brandywine Street, Northwest
Washington, D.C. 20016
202/363-7303

Jul 14, 1986


Pat Vanatta
Hazleton Laboratories
1330-B Piccard Drive
Rockville, MD

Subject: Ophthalmoscopic examination of 80 Rats, Project No. 2399-108
July 9, 1986

All animals examined were found to have no visible lesions
except for the following:

Group I male #8373 Right eye focal zone of retinal degeneration.
Group III Male # 8452 Right eye generalized retinal degener-
ation; left eye early diffuse retinal
degeneration.

Due to the infrequency of abnormal ophthalmoscopic changes,
I do not believe either of these findings to be dose-related.


Nancy M. Bromberg, V.M.D., M.S.
Dip., A.C.V.O.



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- 109 -

APPENDIX 6

Individual Clinical Hematology Values

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- 110 -

KEY TO HEMATOLOGY

Leukocyte Differentials

Blast Cells	BLAST
Metamyelocytes	META
Band Neutrophils	BAND
Segmented Neutrophils	SEG
Lymphocytes	LYMPH
Monocytes	MONO
Eosinophils	EOSIN
Basophils	BASO

Cell Morphology

Echinocytes	ECHINO
Target Cells	TARGET
Hypochromic Cells	HYPO
Poikilocytes	POIK
Acanthocytes	ACANTH
Polychromatophilic Cells	POLY
Nucleated RBC's ^a	NRBC
Howell-Jolly Bodies	HJBODY

Cell morphology findings are graded by the following method.

- = None Present
- T = Trace Numbers Present
- 1 = Slight Numbers Present
- 2 = Moderate Numbers Present
- 3 = Marked Numbers Present
- 4 = Severe Numbers Present

^aExpressed as a percentage of 100 WBC's counted.

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

ANIMAL NUMBER	RBC MI/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC MI/UL
GROUP: 5	DOSE LEVEL: BASELINE					
	DOSAGE UNIT:					
08522	6.74	16.0	43.5	858	6.0	.40
08523	4.75	14.3	29.0	1076	4.2	.20
08524	5.49	14.5	33.7	1328	4.1	.23
08525	5.20	15.3	33.4	1277	5.1	.27
08526	5.23	14.2	32.3	1425	4.0	.21
MEAN	5.48	14.9	34.4	1193	4.7	.26
S.D.	.752	.77	5.43	226.4	.86	.082

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APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	MET TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)
GROUP: 5	DOSE LEVEL: BASELINE								
	UNIT:								
08522	10.1	.0(0)	.0(0)	.0(0)	1.3(13)	8.4(83)	.3(3)	.1(1)	.0(0)
08523	11.1	.0(0)	.0(0)	.0(0)	.4(4)	10.3(93)	.1(1)	.2(2)	.0(0)
08524	16.2	.0(0)	.0(0)	.0(0)	1.1(7)	14.6(90)	.5(3)	.0(0)	.0(0)
08525	16.6	.0(0)	.0(0)	.0(0)	.7(4)	15.3(92)	.7(4)	.0(0)	.0(0)
08526	11.9	.0(0)	.0(0)	.0(0)	.6(5)	10.9(92)	.2(2)	.1(1)	.0(0)
MEAN	13.2	.0	.0	.0	.8	11.9	.4	.1	.0
S.D.	3.01	.00	.00	.00	.37	2.94	.24	.08	.00

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APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	NRBC

GROUP: 5	DOSE LEVEL: BASELINE DOOSAGE UNIT:			
08522	2+	-	4+	1
08523	1+	-	4+	1
08524	3+	-	4+	-
08525	2+	-	4+	2
08526	2+	T	4+	-

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	RBC MI/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC MI/UL
GROUP: 1	DOSE LEVEL: 0	DOSAGE UNIT: MG/KG				
08362	7.83	16.1	43.5	1479	1.7	.13
08363	7.93	15.2	43.8	1207	1.8	.14
08364	7.48	15.1	42.2	1513	1.3	.10
08365	7.90	15.4	46.4	1117	1.6	.13
08366	8.68	16.7	51.1	115	2.7	.23
08367	8.54	16.6	48.2	1211	.3	.03
08368	7.48	14.9	43.0	1178	.7	.05
08369	7.34	14.6	40.3	1271	1.0	.07
08370	6.54	15.8	38.2	930	1.0	.07
08371	6.85	16.1	41.4	989	1.1	.08
MEAN	7.66	15.6	43.8	1101	1.3	.10
S.D.	.671	.72	3.83	392.3	.67	.058
GROUP: 2	DOSE LEVEL: 100	DOSAGE UNIT: MG/KG				
08403	7.89	15.5	47.1	971	1.5	.12
08404	7.83	15.6	46.3	1379	2.8	.22
08405	7.98	15.4	44.8	1206	.8	.06
08406	7.43	15.2	42.3	1288	1.7	.13
08407	7.19	15.7	44.5	1158	2.4	.17
08408	8.06	15.8	46.3	1199	.9	.07
08409	8.26	15.2	46.5	1082	1.6	.13
08410	7.73	15.6	45.1	1297	1.5	.12
08411	6.51	15.0	38.8	1072	1.7	.11
08412	7.73	15.8	42.1	1437	1.6	.12
MEAN	7.66	15.5	44.4	1209	1.6	.12
S.D.	.507	.27	2.60	145.0	.60	.046

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APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	RBC M1/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC M1/UL
GROUP: 3	DOSE LEVEL: 200	DOSAGE UNIT: MG/KG				
08442	7.66	15.4	43.7	1150	.2	.02
08443	7.81	15.3	43.8	1272	1.5	.12
08444	8.04	16.2	45.7	1433	.7	.06
08445	8.04	16.3	45.2	1387	1.1	.09
08447	7.29	15.2	42.6	1210	1.5	.11
08448	8.36	15.3	46.8	1075	1.2	.10
08449	7.75	14.5	43.8	1276	1.7	.13
08450	7.91	15.8	46.0	1333	.8	.06
08451	7.86	16.1	46.4	1122	.9	.07
08452	7.62	15.2	41.3	1153	.9	.07
MEAN	7.83	15.5	44.5	1241	1.0	.08
S.D.	.288	.56	1.78	119.0	.45	.033
GROUP: 4	DOSE LEVEL: 800	DOSAGE UNIT: MG/KG				
08482	7.42	15.5	42.6	1111	1.5	.11
08483	7.46	15.4	41.8	1159	1.3	.10
08484	8.19	15.9	47.0	1221	1.4	.11
08485	7.40	15.1	42.1	1076	1.6	.12
08486	6.98	15.6	40.3	1194	.9	.06
08487	7.62	15.8	44.2	1147	1.5	.11
08488	7.27	14.4	40.3	1395	1.7	.12
08489	8.60	17.0	47.5	NO TEST	1.2	.10
08490	7.20	16.0	41.1	1226	1.5	.11
08491	7.18	15.8	40.3	1213	1.2	.09
MEAN	7.53	15.6	42.7	1194	1.4	.10
S.D.	.497	.67	2.68	91.4	.23	.018

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	MET TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)
GROUP: 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG									
08362	15.0	.0(0)	.0(0)	.0(0)	1.8(12)	12.9(86)	.3(2)	.0(0)	.0(0)
08363	10.2	.0(0)	.0(0)	.0(0)	.5(5)	9.7(95)	.0(0)	.0(0)	.0(0)
08364	21.5	.0(0)	.0(0)	.2(1)	3.4(16)	17.6(82)	.0(0)	.2(1)	.0(0)
08365	17.3	.0(0)	.0(0)	.0(0)	1.9(11)	15.4(89)	.0(0)	.0(0)	.0(0)
08366	12.9	.0(0)	.0(0)	.0(0)	7.4(57)	5.5(43)	.0(0)	.0(0)	.0(0)
08367	13.4	.0(0)	.0(0)	.0(0)	.8(6)	12.5(93)	.0(0)	.1(1)	.0(0)
08368	17.1	.0(0)	.0(0)	.0(0)	2.6(15)	13.9(81)	.3(2)	.3(2)	.0(0)
08369	16.3	.0(0)	.0(0)	.0(0)	2.3(14)	13.9(85)	.0(0)	.2(1)	.0(0)
08370	19.8	.0(0)	.0(0)	.0(0)	2.2(11)	17.6(89)	.0(0)	.0(0)	.0(0)
08371	19.3	.0(0)	.0(0)	.0(0)	2.7(14)	16.4(85)	.2(1)	.0(0)	.0(0)
MEAN	16.3	.0	.0	.0	2.6	13.5	.1	.1	.0
S.D.	3.48	.00	.00	.06	1.91	3.74	.13	.11	.00
GROUP: 2 DOSE LEVEL: 100 DOSAGE UNIT: MG/KG									
08403	9.8	.0(0)	.0(0)	.1(1)	1.1(11)	8.5(87)	.0(0)	.1(1)	.0(0)
08404	11.7	.0(0)	.0(0)	.0(0)	2.8(24)	8.4(72)	.1(1)	.4(3)	.0(0)
08405	14.0	.0(0)	.0(0)	.0(0)	1.8(13)	12.2(87)	.0(0)	.0(0)	.0(0)
08406	13.5	.0(0)	.0(0)	.0(0)	.7(5)	12.3(91)	.3(2)	.3(2)	.0(0)
08407	15.7	.0(0)	.0(0)	.0(0)	2.7(17)	12.7(81)	.0(0)	.3(2)	.0(0)
08408	19.0	.0(0)	.0(0)	.0(0)	1.5(8)	17.1(90)	.0(0)	.4(2)	.0(0)
08409	17.7	.0(0)	.0(0)	.0(0)	1.1(6)	16.5(93)	.2(1)	.0(0)	.0(0)
08410	12.4	.0(0)	.0(0)	.0(0)	2.0(16)	9.7(78)	.2(2)	.5(4)	.0(0)
08411	19.6	.0(0)	.0(0)	.0(0)	3.5(18)	15.5(79)	.2(1)	.4(2)	.0(0)
08412	19.2	.0(0)	.0(0)	.0(0)	1.7(9)	17.3(90)	.2(1)	.0(0)	.0(0)
MEAN	15.3	.0	.0	.0	1.9	13.0	.1	.2	.0
S.D.	3.49	.00	.00	.03	.88	3.45	.11	.20	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL (%)	MET TH/UL (%)	BAND TH/UL (%)	SEG TH/UL (%)	LYMPH TH/UL (%)	MONO TH/UL (%)	EOSIN TH/UL (%)	BASO TH/UL (%)
GROUP: 3	DOSE LEVEL: 200								
	DOSAGE UNIT: MG/KG								
08442	8.6	.0(0)	.0(0)	.0(0)	1.2(14)	7.1(83)	.0(0)	.3(3)	.0(0)
08443	11.7	.0(0)	.0(0)	.0(0)	1.5(13)	10.1(86)	.0(0)	.1(1)	.0(0)
08444	16.4	.0(0)	.0(0)	.0(0)	3.1(19)	12.6(77)	.5(3)	.2(1)	.0(0)
08445	19.4	.0(0)	.0(0)	.0(0)	3.1(16)	15.9(82)	.0(0)	.4(2)	.0(0)
08447	26.2	.0(0)	.0(0)	.0(0)	4.2(16)	21.5(82)	.0(0)	.5(2)	.0(0)
08448	21.1	.0(0)	.0(0)	.0(0)	1.3(6)	19.0(90)	.4(2)	.4(2)	.0(0)
08449	16.9	.0(0)	.0(0)	.0(0)	4.7(28)	11.7(69)	.2(1)	.3(2)	.0(0)
08450	22.5	.0(0)	.0(0)	.0(0)	2.9(13)	19.6(87)	.0(0)	.0(0)	.0(0)
08451	18.0	.0(0)	.0(0)	.0(0)	3.8(21)	13.9(77)	.4(2)	.0(0)	.0(0)
08452	23.2	.0(0)	.0(0)	.0(0)	.5(2)	22.5(97)	.2(1)	.0(0)	.0(0)
MEAN	18.4	.0	.0	.0	2.6	15.4	.2	.2	.0
S.D.	5.34	.00	.00	.00	1.42	5.16	.20	.19	.00
GROUP: 4	DOSE LEVEL: 800								
	DOSAGE UNIT: MG/KG								
08482	11.8	.0(0)	.0(0)	.0(0)	2.8(24)	8.6(73)	.2(2)	.1(1)	.0(0)
08483	15.7	.0(0)	.0(0)	.2(1)	.8(5)	14.4(92)	.2(1)	.2(1)	.0(0)
08484	14.3	.0(0)	.0(0)	.0(0)	3.4(24)	10.7(75)	.1(1)	.0(0)	.0(0)
08485	18.1	.0(0)	.0(0)	.0(0)	1.6(9)	16.3(90)	.0(0)	.2(1)	.0(0)
08486	12.2	.0(0)	.0(0)	.0(0)	1.8(15)	10.2(84)	.0(0)	.1(1)	.0(0)
08487	23.7	.0(0)	.0(0)	.0(0)	3.3(14)	19.4(82)	.5(2)	.5(2)	.0(0)
08488	24.0	.0(0)	.0(0)	.0(0)	6.2(26)	17.3(72)	.5(2)	.0(0)	.0(0)
08489	20.6	.0(0)	.0(0)	.0(0)	1.6(8)	18.3(89)	.0(0)	.6(3)	.0(0)
08490	14.3	.0(0)	.0(0)	.0(0)	1.3(9)	12.6(88)	.0(0)	.4(3)	.0(0)
08491	18.0	.0(0)	.0(0)	.0(0)	2.2(12)	15.1(84)	.2(1)	.5(3)	.0(0)
MEAN	17.3	.0	.0	.0	2.5	14.3	.2	.3	.0
S.D.	4.41	.00	.00	.06	1.55	3.66	.19	.22	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	HJBODY	POIK	NRBC
GROUP: 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG							
08362	T	-	3+	T	-	-	-
08363	T	-	2+	-	-	-	-
08364	T	-	4+	-	-	-	-
08365	1+	T	3+	-	-	-	-
08366	T	-	3+	-	-	-	-
08367	T	-	3+	-	1+	-	-
08368	T	-	2+	T	-	-	-
08369	T	-	4+	-	1+	-	-
08370	T	-	4+	-	-	-	-
08371	T	-	4+	-	-	-	-
GROUP: 2 DOSE LEVEL: 100 DOSAGE UNIT: MG/KG							
08403	1+	-	2+	-	-	-	-
08404	1+	-	2+	-	-	-	-
08405	T	1+	3+	T	-	-	-
08406	T	T	4+	-	-	-	-
08407	T	T	4+	-	-	-	-
08408	T	-	2+	-	-	-	-
08409	T	-	2+	-	-	-	-
08410	T	-	2+	-	-	-	1
08411	T	-	4+	T	-	-	-
08412	T	-	4+	-	-	-	-
GROUP: 3 DOSE LEVEL: 200 DOSAGE UNIT: MG/KG							
08442	T	-	3+	-	-	-	-
08443	T	-	4+	T	-	-	-
08444	T	1+	3+	-	-	-	-
08445	T	-	4+	-	-	-	-
08447	T	1+	4+	-	-	-	-
08448	T	-	1+	-	T	-	-
08449	T	-	2+	T	-	-	-
08450	T	-	3+	-	T	-	-
08451	T	-	3+	-	-	-	-
08452	T	-	4+	-	-	-	-

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	HJBODY	POIK	NRBC
GROUP: 4		DOSE LEVEL: 800		DOSAGE UNIT: MG/KG			
08482	T	-	3+	-	-	-	-
08483	T	T	4+	-	-	-	-
08484	T	1+	3+	-	-	-	-
08485	T	-	4+	-	-	-	-
08486	T	T	4+	-	-	-	-
08487	T	-	2+	-	-	-	-
08488	T	-	2+	-	-	-	-
08489	T	-	3+	-	-	-	-
08490	T	-	4+	-	-	-	-
08491	T	-	4+	-	-	-	-

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	RBC M1/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC M1/UL
GROUP: 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG						
08362	8.31	15.4	41.9	1272	1.5	.12
08363	8.83	16.0	44.2	1138	1.1	.10
08364	8.30	15.1	41.7	1385	1.1	.09
08365	8.60	15.8	43.9	1011	1.1	.09
08366	8.47	15.5	43.4	1327	.7	.06
08367	8.35	15.5	42.8	1299	1.0	.08
08368	8.66	16.1	45.2	1198	.7	.06
08369	8.39	15.3	41.4	1392	1.1	.09
08370	8.84	16.3	45.4	996	.5	.04
08371	8.00	15.8	44.0	793	.7	.06
MEAN	8.47	15.7	43.4	1181	.9	.08
S.D.	.262	.38	1.41	195.9	.30	.024
GROUP: 2 DOSE LEVEL: 100 DOSAGE UNIT: MG/KG						
08403	8.77	16.7	46.8	1033	.8	.07
08404	8.42	15.9	43.7	1254	2.5	.21
08405	7.78	13.9	38.8	1351	1.3	.10
08406	8.74	16.1	44.7	1087	1.6	.14
08407	8.08	16.0	45.8	1069	2.3	.19
08408	8.53	15.6	43.8	1040	.2	.02
08409	8.84	15.5	43.8	969	1.0	.09
08410	8.39	15.8	43.5	1032	1.1	.09
08411	8.47	16.2	45.0	1058	1.3	.11
08412	8.97	15.9	43.5	1239	.6	.05
MEAN	8.50	15.8	43.9	1113	1.3	.11
S.D.	.362	.73	2.11	123.4	.71	.059

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC-TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	RBC MI/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC MI/UL
GROUP: 3	DOSE LEVEL: 200			DOSAGE UNIT: MG/KG		
08442	8.77	16.4	45.6	1038	.9	.08
08443	8.94	16.1	45.0	1126	3.5	.31
08444	8.66	16.0	44.6	1297	1.6	.14
08445	8.81	16.2	44.7	1362	2.0	.18
08447	8.07	15.1	42.1	1199	3.5	.28
08449	8.41	14.8	42.7	1137	.5	.04
08451	8.50	15.9	45.0	1069	.8	.07
08452	9.14	16.1	44.9	1006	.2	.02
08453	7.93	14.7	41.2	1067	.9	.07
08455	8.64	16.0	44.0	1257	.7	.06
MEAN	8.59	15.7	44.0	1156	1.5	.12
S.D.	.374	.62	1.47	119.0	1.19	.101
GROUP: 4	DOSE LEVEL: 800			DOSAGE UNIT: MG/KG		
08482	8.04	15.1	42.2	885	1.8	.14
08483	8.53	16.1	44.4	1070	1.3	.11
08484	8.89	15.7	45.1	1159	.5	.04
08485	8.49	15.6	43.5	1026	2.6	.22
08486	8.57	16.0	44.7	1122	1.8	.15
08487	8.60	16.6	46.2	1139	1.6	.14
08488	6.45	11.6	32.7	1388	.7	.05
08489	9.48	17.0	47.8	1115	.3	.03
08490	8.77	16.7	46.0	1076	.8	.07
08492	9.24	17.1	46.7	1054	.2	.02
MEAN	8.51	15.7	43.9	1103	1.2	.10
S.D.	.827	1.59	4.26	126.4	.78	.065

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC-TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL (%)	MET TH/UL (%)	BAND TH/UL (%)	SEG TH/UL (%)	LYMPH TH/UL (%)	MONO TH/UL (%)	EOSIN TH/UL (%)	BASO TH/UL (%)
GROUP: 1	DOSE LEVEL: 0								
	DOSAGE UNIT: MG/KG								
08362	13.3	.0(0)	.0(0)	.0(0)	2.7(20)	10.4(78)	.1(1)	.1(1)	.0(0)
08363	11.3	.0(0)	.0(0)	.0(0)	.5(4)	10.8(96)	.0(0)	.0(0)	.0(0)
08364	21.9	.0(0)	.0(0)	.0(0)	2.8(13)	18.4(84)	.4(2)	.2(1)	.0(0)
08365	17.1	.0(0)	.0(0)	.0(0)	1.0(6)	15.7(92)	.2(1)	.2(1)	.0(0)
08366	16.2	.0(0)	.0(0)	.0(0)	3.4(21)	12.8(79)	.0(0)	.0(0)	.0(0)
08367	16.8	.0(0)	.0(0)	.0(0)	3.9(23)	12.9(77)	.0(0)	.0(0)	.0(0)
08368	16.6	.0(0)	.0(0)	.0(0)	2.8(17)	13.8(83)	.0(0)	.0(0)	.0(0)
08369	12.7	.0(0)	.0(0)	.0(0)	1.8(14)	10.8(85)	.0(0)	.1(1)	.0(0)
08370	15.8	.0(0)	.0(0)	.0(0)	3.5(22)	12.2(77)	.0(0)	.2(1)	.0(0)
08371	21.0	.0(0)	.0(0)	.0(0)	2.9(14)	18.1(86)	.0(0)	.0(0)	.0(0)
MEAN	16.3	.0	.0	.0	2.5	13.6	.1	.1	.0
S.D.	3.36	.00	.00	.00	1.10	2.92	.13	.09	.00
GROUP: 2	DOSE LEVEL: 100								
	DOSAGE UNIT: MG/KG								
08403	14.9	.0(0)	.0(0)	.0(0)	1.3(9)	13.6(91)	.0(0)	.0(0)	.0(0)
08404	10.1	.0(0)	.0(0)	.0(0)	1.4(14)	8.6(85)	.1(1)	.0(0)	.0(0)
08405	20.0	.0(0)	.0(0)	.0(0)	7.6(38)	12.4(82)	.0(0)	.0(0)	.0(0)
08406	10.7	.0(0)	.0(0)	.0(0)	1.6(15)	9.1(85)	.0(0)	.0(0)	.0(0)
08407	13.7	.0(0)	.0(0)	.0(0)	3.0(22)	10.3(75)	.0(0)	.4(3)	.0(0)
08408	16.3	.0(0)	.0(0)	.0(0)	.5(3)	15.8(97)	.0(0)	.0(0)	.0(0)
08409	12.2	.0(0)	.0(0)	.0(0)	.4(3)	11.7(96)	.0(0)	.1(1)	.0(0)
08410	10.9	.0(0)	.0(0)	.0(0)	1.7(16)	8.7(80)	.1(1)	.3(3)	.0(0)
08411	20.4	.0(0)	.0(0)	.0(0)	4.7(23)	15.3(75)	.2(1)	.2(1)	.0(0)
08412	16.1	.0(0)	.0(0)	.0(0)	1.4(9)	14.5(90)	.0(0)	.2(1)	.0(0)
MEAN	14.5	.0	.0	.0	2.4	12.0	.0	.1	.0
S.D.	3.71	.00	.00	.00	2.23	2.75	.07	.15	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC-TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL (%)	MET TH/UL (%)	BAND TH/UL (%)	SEG TH/UL (%)	LYMPH TH/UL (%)	MONO TH/UL (%)	EOSIN TH/UL (%)	BASO TH/UL (%)
GROUP: 3	DOSE LEVEL: 200								
08442	13.5	.0(0)	.0(0)	.0(0)	1.3(10)	11.6(86)	.3(2)	.3(2)	.0(0)
08443	15.6	.0(0)	.0(0)	.0(0)	1.4(9)	14.0(90)	.0(0)	.2(1)	.0(0)
08444	15.9	.0(0)	.0(0)	.0(0)	3.2(20)	12.6(79)	.0(0)	.2(1)	.0(0)
08445	14.1	.0(0)	.0(0)	.0(0)	2.1(15)	11.7(83)	.1(1)	.1(1)	.0(0)
08447	24.4	.0(0)	.0(0)	.0(0)	6.8(28)	17.3(71)	.2(1)	.0(0)	.0(0)
08449	15.1	.0(0)	.0(0)	.0(0)	2.4(16)	12.5(83)	.0(0)	.2(1)	.0(0)
08451	13.3	.0(0)	.0(0)	.0(0)	1.5(11)	11.7(88)	.0(0)	.1(1)	.0(0)
08452	17.7	.0(0)	.0(0)	.0(0)	.7(4)	16.6(94)	.0(0)	.4(2)	.0(0)
08453	19.5	.0(0)	.0(0)	.0(0)	3.9(20)	15.4(79)	.0(0)	.2(1)	.0(0)
08455	23.6	.0(0)	.0(0)	.0(0)	4.0(17)	19.1(81)	.0(0)	.5(2)	.0(0)
MEAN	17.3	.0	.0	.0	2.7	14.2	.1	.2	.0
S.D.	4.02	.00	.00	.00	1.82	2.70	.11	.15	.00
GROUP: 4	DOSE LEVEL: 800								
08482	11.0	.0(0)	.0(0)	.0(0)	2.4(22)	8.4(76)	.0(0)	.2(2)	.0(0)
08483	15.2	.0(0)	.0(0)	.0(0)	.9(6)	14.1(93)	.2(1)	.0(0)	.0(0)
08484	17.3	.0(0)	.0(0)	.0(0)	4.3(25)	12.6(73)	.2(1)	.2(1)	.0(0)
08485	22.9	.0(0)	.0(0)	.0(0)	2.3(10)	20.6(90)	.0(0)	.0(0)	.0(0)
08486	9.6	.0(0)	.0(0)	.0(0)	1.2(13)	8.4(87)	.0(0)	.0(0)	.0(0)
08487	18.0	.0(0)	.0(0)	.0(0)	2.9(16)	14.8(82)	.0(0)	.4(2)	.0(0)
08488	20.5	.0(0)	.0(0)	.0(0)	5.3(26)	15.0(73)	.2(1)	.0(0)	.0(0)
08489	21.9	.0(0)	.0(0)	.0(0)	1.3(6)	20.4(93)	.0(0)	.2(1)	.0(0)
08490	12.3	.0(0)	.0(0)	.0(0)	.9(7)	11.1(90)	.0(0)	.4(3)	.0(0)
08492	17.4	.0(0)	.0(0)	.0(0)	2.8(16)	14.4(83)	.0(0)	.2(1)	.0(0)
MEAN	16.6	.0	.0	.0	2.4	14.0	.1	.2	.0
S.D.	4.56	.00	.00	.00	1.48	4.21	.10	.16	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC-TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	POLY	TARGET	ECHIND	ACANTH	POIK
<hr/>					
GROUP: 1	DOSE LEVEL: 0		DOSAGE UNIT: MG/KG		
08362	T	-	1+	T	-
08363	T	-	T	-	-
08364	T	-	T	T	-
08365	T	-	T	-	-
08366	T	-	T	-	T
08367	T	-	3+	T	-
08368	T	-	T	T	-
08369	T	-	1+	T	T
08370	T	-	T	-	-
08371	T	-	-	-	-
GROUP: 2	DOSE LEVEL: 100		DOSAGE UNIT: MG/KG		
08403	T	-	-	-	-
08404	T	-	T	-	-
08405	T	-	1+	T	-
08406	T	-	T	1+	-
08407	T	-	T	-	-
08408	T	-	1+	T	-
08409	T	-	T	-	T
08410	T	-	T	-	-
08411	T	-	T	-	T
08412	T	-	1+	-	T
GROUP: 3	DOSE LEVEL: 200		DOSAGE UNIT: MG/KG		
08442	T	-	T	-	-
08443	T	-	T	-	-
08444	T	-	T	-	-
08445	T	-	T	-	-
08447	T	-	T	-	-
08449	T	-	T	-	-
08451	T	T	T	-	-
08452	T	-	T	-	T
08453	T	-	T	-	-
08455	T	-	T	-	-

HLA 2399108

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	POLY	TARGET	EDHNO	ACANTH	POIK

GROUP: 4	DOSE LEVEL: 800		DOSAGE UNIT: MG/KG		
08482	T	-	T	-	-
08483	T	-	T	-	-
08484	T	-	T	-	-
08485	T	-	T	T	-
08486	T	-	T	-	-
08487	T	-	T	-	-
08488	T	T	1+	-	-
08489	T	-	T	-	-
08490	T	-	-	-	-
08492	T	-	T	-	-

HLA 2399108

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

ANIMAL NUMBER	RBC M/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC M/UL
GROUP: 5	DOSE LEVEL: BASELINE					
	DOSAGE UNIT:					
08527	5.18	15.7	32.7	1227	4.9	.25
08528	3.50	14.8	23.2	1364	4.2	.15
08529	4.80	14.8	29.4	1430	5.3	.25
08530	4.62	15.8	29.0	1429	3.8	.18
08531	4.58	15.1	28.8	1311	5.0	.23
MEAN	4.54	15.2	28.6	1352	4.6	.21
S.D.	.626	.48	3.42	85.8	.62	.045

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL (%)	MET TH/UL (%)	BAND TH/UL (%)	SEG TH/UL (%)	LYMPH TH/UL (%)	MONO TH/UL (%)	EOSIN TH/UL (%)	BASO TH/UL (%)
GROUP: 5	DOSE LEVEL: BASELINE								
08527	18.2	.0(0)	.0(0)	.0(0)	.5(3)	16.9(93)	.5(3)	.2(1)	.0(0)
08528	17.9	.0(0)	.0(0)	.0(0)	1.4(8)	16.1(90)	.4(2)	.0(0)	.0(0)
08529	12.8	.0(0)	.0(0)	.0(0)	.8(6)	11.9(93)	.0(0)	.1(1)	.0(0)
08530	14.4	.0(0)	.0(0)	.0(0)	1.7(12)	12.1(84)	.4(3)	.1(1)	.0(0)
08531	13.6	.0(0)	.0(0)	.0(0)	1.0(7)	12.0(88)	.1(1)	.5(4)	.0(0)
MEAN	15.4	.0	.0	.0	1.1	13.8	.3	.2	.0
S.D.	2.50	.00	.00	.00	.48	2.48	.22	.19	.00

HLA 2399108

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	NRBC
GROUP: 5	DOSE LEVEL: BASELINE			
08527	1+	T	4+	-
08528	1+	-	1+	-
08529	2+	-	4+	-
08530	1+	-	1+	-
08531	2+	-	4+	-

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	RBC M1/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC M1/UL
GROUP: 1	DOSE LEVEL: 0			DOSAGE UNIT: MG/KG		
08382	5.88	14.8	34.1	1311	1.0	.06
08383	7.74	15.4	44.5	1311	1.1	.09
08384	7.37	15.3	42.7	1211	1.8	.13
08385	6.85	13.8	37.9	1182	1.3	.09
08386	6.69	15.7	37.4	1201	.7	.05
08387	7.76	15.4	43.7	1191	.9	.07
08388	8.00	15.5	45.8	1201	.6	.05
08389	7.41	15.2	42.3	1102	1.3	.10
08390	6.50	14.5	37.4	1319	.6	.04
08391	6.34	15.0	35.2	1224	.8	.05
MEAN	7.05	15.1	40.1	1225	1.0	.07
S.D.	.704	.57	4.16	69.2	.38	.029
GROUP: 2	DOSE LEVEL: 100			DOSAGE UNIT: MG/KG		
08422	6.63	14.6	38.7	1400	1.4	.09
08423	5.94	15.4	33.6	1320	1.9	.11
08424	7.68	16.0	45.0	1484	1.3	.10
08425	7.75	15.7	44.1	1415	2.2	.17
08426	6.40	15.9	37.6	1157	1.3	.08
08427	6.71	15.5	39.3	1330	1.1	.07
08428	7.84	15.6	46.5	1354	1.2	.09
08429	7.01	15.1	40.8	1363	3.1	.22
08430	7.01	15.0	38.3	1233	.3	.02
08431	6.62	15.0	36.6	1115	.6	.04
MEAN	6.96	15.4	40.0	1317	1.4	.10
S.D.	.629	.45	4.06	116.2	.80	.059

HLA 2399108

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	RBC MI/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC MI/UL
GROUP: 3	DOSE LEVEL: 200	DOSE UNIT: MG/KG				
08462	6.19	15.1	36.0	1300	1.3	.08
08463	7.87	16.0	44.6	1318	1.2	.09
08464	7.42	15.9	41.6	1358	.6	.04
08465	6.50	15.6	39.2	1174	1.1	.07
08466	6.64	16.5	38.8	1322	1.0	.07
08467	7.87	16.0	46.5	1186	1.0	.08
08469	7.21	14.2	40.8	1434	1.0	.07
08470	6.95	14.5	39.0	1161	1.0	.07
08471	6.26	15.2	35.8	1043	.6	.04
08472	6.46	14.6	36.6	1463	1.0	.06
MEAN	6.94	15.4	39.9	1276	1.0	.07
S.D.	.630	.76	3.57	132.1	.23	.016
GROUP: 4	DOSE LEVEL: 800	DOSE UNIT: MG/KG				
08502	6.85	15.0	37.8	1201	1.2	.08
08503	6.21	15.2	33.6	1252	1.2	.07
08504	6.63	15.2	37.2	1353	1.2	.08
08506	6.16	14.3	34.1	1406	1.0	.06
08507	5.84	16.2	35.4	1086	1.8	.11
08508	6.61	15.3	36.6	1206	1.4	.09
08509	5.26	14.8	30.1	1118	.9	.05
08510	7.01	15.6	38.5	1243	1.8	.13
08511	6.90	16.5	38.7	1329	.9	.06
08512	6.72	15.3	37.6	1271	1.4	.09
MEAN	6.42	15.3	36.0	1247	1.3	.08
S.D.	.550	.64	2.70	100.1	.33	.024

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)
GROUP: 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG									
08382	13.0	.0(0)	.0(0)	.0(0)	2.3(18)	10.3(79)	.3(2)	.1(1)	.0(0)
08383	8.0	.0(0)	.0(0)	.1(1)	1.7(21)	6.1(76)	.2(2)	.0(0)	.0(0)
08384	9.9	.0(0)	.0(0)	.0(0)	1.0(10)	8.6(87)	.1(1)	.2(2)	.0(0)
08385	13.9	.0(0)	.0(0)	.0(0)	4.2(30)	9.5(68)	.1(1)	.1(1)	.0(0)
08386	16.6	.0(0)	.0(0)	.0(0)	2.0(12)	14.6(88)	.0(0)	.0(0)	.0(0)
08387	16.2	.0(0)	.0(0)	.0(0)	2.6(16)	13.3(82)	.0(0)	.3(2)	.0(0)
08388	13.4	.0(0)	.0(0)	.0(0)	2.0(15)	11.0(82)	.3(2)	.1(1)	.0(0)
08389	14.2	.0(0)	.0(0)	.0(0)	1.6(11)	12.1(89)	.1(1)	.4(3)	.0(0)
08390	21.1	.0(0)	.0(0)	.0(0)	2.3(11)	18.6(88)	.0(0)	.2(1)	.0(0)
08391	13.5	.0(0)	.0(0)	.0(0)	2.3(17)	10.9(81)	.1(1)	.1(1)	.0(0)
MEAN	14.0	.0	.0	.0	2.2	11.5	.1	.1	.0
S.D.	3.60	.00	.00	.03	.84	3.45	.11	.13	.00
GROUP: 2 DOSE LEVEL: 100 DOSAGE UNIT: MG/KG									
08422	10.5	.0(0)	.0(0)	.0(0)	2.5(24)	7.6(72)	.3(3)	.1(1)	.0(0)
08423	13.1	.0(0)	.0(0)	.0(0)	1.3(10)	11.5(88)	.1(1)	.1(1)	.0(0)
08424	11.9	.0(0)	.0(0)	.0(0)	1.8(15)	9.9(83)	.0(0)	.2(2)	.0(0)
08425	15.1	.0(0)	.0(0)	.0(0)	3.8(25)	11.2(74)	.0(0)	.2(1)	.0(0)
08426	14.3	.0(0)	.0(0)	.0(0)	.7(5)	13.3(93)	.1(1)	.1(1)	.0(0)
08427	22.7	.0(0)	.0(0)	.2(1)	2.5(11)	19.1(84)	.5(2)	.5(2)	.0(0)
08428	16.6	.0(0)	.0(0)	.0(0)	1.3(8)	14.6(88)	.0(0)	.7(4)	.0(0)
08429	12.0	.0(0)	.0(0)	.0(0)	3.0(25)	9.0(75)	.0(0)	.0(0)	.0(0)
08430	11.1	.0(0)	.0(0)	.0(0)	.8(7)	10.1(91)	.1(1)	.1(1)	.0(0)
08431	10.6	.0(0)	.0(0)	.0(0)	1.3(12)	9.1(86)	.0(0)	.2(2)	.0(0)
MEAN	13.8	.0	.0	.0	1.9	11.5	.1	.2	.0
S.D.	3.72	.00	.00	.06	1.02	3.37	.17	.21	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL (%)	MET TH/UL (%)	BAND TH/UL (%)	SEG TH/UL (%)	LYMPH TH/UL (%)	MONO TH/UL (%)	EOSIN TH/UL (%)	BASO TH/UL (%)
GROUP: 3	DOSE LEVEL: 200								
	DOSAGE UNIT: MG/KG								
08462	10.2	.0(0)	.0(0)	.0(0)	1.0(10)	8.7(85)	.1(1)	.4(4)	.0(0)
08463	10.1	.0(0)	.0(0)	.1(1)	2.1(21)	7.8(77)	.0(0)	.1(1)	.0(0)
08464	11.6	.0(0)	.0(0)	.0(0)	2.4(21)	8.8(76)	.0(0)	.3(3)	.0(0)
08465	12.6	.0(0)	.0(0)	.0(0)	1.6(13)	10.7(85)	.3(2)	.0(0)	.0(0)
08466	18.9	.0(0)	.0(0)	.0(0)	2.1(11)	16.8(89)	.0(0)	.0(0)	.0(0)
08467	16.0	.0(0)	.0(0)	.0(0)	1.1(7)	14.6(91)	.2(1)	.2(1)	.0(0)
08469	15.4	.0(0)	.0(0)	.0(0)	1.5(10)	12.9(84)	.3(2)	.6(4)	.0(0)
08470	12.5	.0(0)	.0(0)	.0(0)	1.4(11)	11.0(88)	.0(0)	.1(1)	.0(0)
08471	19.5	.0(0)	.0(0)	.0(0)	1.8(9)	17.7(91)	.0(0)	.0(0)	.0(0)
08472	16.3	.0(0)	.0(0)	.0(0)	3.3(20)	12.7(78)	.3(2)	.0(0)	.0(0)
MEAN	14.3	.0	.0	.0	1.8	12.2	.1	.2	.0
S.D.	3.40	.00	.00	.03	.68	3.41	.14	.21	.00
GROUP: 4	DOSE LEVEL: 800								
	DOSAGE UNIT: MG/KG								
08502	9.8	.0(0)	.0(0)	.0(0)	1.0(10)	8.4(86)	.3(3)	.1(1)	.0(0)
08503	14.1	.0(0)	.0(0)	.0(0)	1.0(7)	13.0(92)	.0(0)	.1(1)	.0(0)
08504	18.6	.0(0)	.0(0)	.0(0)	2.2(12)	15.8(85)	.2(1)	.4(2)	.0(0)
08506	12.1	.0(0)	.0(0)	.0(0)	2.4(20)	9.6(79)	.0(0)	.1(1)	.0(0)
08507	13.8	.0(0)	.0(0)	.0(0)	.8(6)	13.0(94)	.0(0)	.0(0)	.0(0)
08508	16.1	.0(0)	.0(0)	.0(0)	2.6(16)	12.4(77)	.6(4)	.5(3)	.0(0)
08509	18.2	.0(0)	.0(0)	.0(0)	.4(2)	17.5(96)	.0(0)	.4(2)	.0(0)
08510	14.5	.0(0)	.0(0)	.0(0)	1.6(11)	12.6(87)	.1(1)	.1(1)	.0(0)
08511	18.0	.0(0)	.0(0)	.0(0)	2.0(11)	15.8(88)	.0(0)	.2(1)	.0(0)
08512	13.4	.0(0)	.0(0)	.0(0)	1.3(10)	11.7(87)	.4(3)	.0(0)	.0(0)
MEAN	14.9	.0	.0	.0	1.5	13.0	.2	.2	.0
S.D.	2.86	.00	.00	.00	.75	2.81	.21	.18	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	HJBODY	POIK	NRBC

GROUP: 1	DOSE LEVEL: 0		DOSAGE UNIT: MG/KG				
08382	T	-	4+	-	-	-	-
08383	T	-	3+	-	-	-	-
08384	T	1+	4+	-	-	-	-
08385	1+	1+	4+	-	-	-	-
08386	T	-	4+	-	-	-	-
08387	T	-	3+	-	-	-	-
08388	T	-	1+	-	-	-	-
08389	T	-	3+	-	-	-	-
08390	T	-	4+	-	-	-	-
08391	T	-	4+	-	-	-	-
GROUP: 2	DOSE LEVEL: 100		DOSAGE UNIT: MG/KG				
08422	T	-	4+	-	-	-	-
08423	T	-	4+	-	-	-	-
08424	T	-	4+	-	-	-	-
08425	T	-	4+	-	-	-	-
08426	T	-	4+	-	-	-	-
08427	T	-	4+	-	-	-	-
08428	T	-	3+	-	-	-	-
08429	T	-	4+	-	-	-	-
08430	T	-	3+	-	-	-	-
08431	T	-	4+	-	-	-	-
GROUP: 3	DOSE LEVEL: 200		DOSAGE UNIT: MG/KG				
08462	T	-	4+	-	-	-	-
08463	T	-	4+	-	-	-	-
08464	T	T	4+	-	-	-	-
08465	T	-	4+	-	-	-	-
08466	T	-	4+	-	-	-	-
08467	T	-	3+	-	-	-	-
08469	T	-	3+	-	-	T	-
08470	T	-	4+	-	-	-	-
08471	T	-	4+	-	-	-	-
08472	1+	T	4+	-	-	-	-

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	HJBODY	POIK	NRBC
GROUP: 4	DOSE LEVEL: 800				DOSAGE UNIT: MG/KG		
08502	T	-	4+	-	-	-	-
08503	T	-	4+	-	FEW	-	-
08504	T	1+	4+	-	-	-	-
08506	T	-	4+	-	-	-	-
08507	T	-	4+	-	-	-	-
08508	T	-	4+	-	-	-	-
08509	T	-	4+	-	-	-	-
08510	T	-	4+	-	-	-	-
08511	T	-	4+	-	-	-	-
08512	T	-	4+	-	-	-	-

HLA 2399108

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	RBC MI/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC MI/UL
GROUP: 1	DOSE LEVEL: 0			DOSAGE UNIT: MG/KG		
08382	8.20	15.5	44.9	1246	1.5	.12
08383	8.16	15.6	44.5	1127	2.4	.20
08384	8.15	16.1	44.7	1086	1.5	.12
08385	7.74	14.1	40.2	1019	.5	.04
08386	8.39	16.3	44.5	1094	1.6	.13
08387	8.59	16.2	44.7	1121	.4	.03
08388	7.91	14.8	42.2	1147	.5	.04
08389	8.36	15.9	45.2	1015	.8	.07
08390	8.13	15.3	42.9	1468	.2	.02
08391	7.89	15.1	41.9	1094	1.0	.08
MEAN	8.15	15.5	43.6	1142	1.0	.08
S.D.	.256	.69	1.67	132.0	.69	.057
GROUP: 2	DOSE LEVEL: 100			DOSAGE UNIT: MG/KG		
08422	7.88	15.1	42.6	1141	2.1	.17
08423	7.99	15.3	41.9	1206	3.2	.26
08424	8.27	16.2	44.4	1141	.7	.06
08425	8.13	15.6	43.6	1275	.9	.07
08426	8.38	16.7	46.0	1175	1.2	.10
08427	7.99	15.5	42.8	1152	.6	.05
08428	7.83	15.6	44.2	1187	.3	.02
08429	7.86	15.1	42.1	1333	.6	.05
08430	8.58	15.6	44.3	1067	.7	.06
08431	8.37	16.0	44.4	882	.3	.03
MEAN	8.13	15.7	43.6	1156	1.1	.09
S.D.	.260	.50	1.28	121.5	.92	.074

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	RBC MI/UL	HGB G/DL	HCT %	PLATELET TH/UL	RETIC % RBC	A RETIC MI/UL
GROUP: 3 DOSE LEVEL: 200 DOSAGE UNIT: MG/KG						
08462	7.72	15.4	42.3	1057	1.9	.15
08463	8.48	16.1	44.5	1450	.6	.05
08464	8.68	16.6	45.7	1126	.6	.05
08465	7.92	15.6	44.3	1199	2.4	.19
08466	8.53	16.7	47.1	1178	2.3	.20
08467	8.03	15.5	44.4	784	1.5	.12
08469	8.23	15.1	42.3	1484	.6	.05
08470	8.20	15.5	43.1	1057	.7	.06
08471	8.19	15.8	44.3	1220	.6	.05
08472	8.29	15.5	44.0	1283	.4	.03
MEAN	8.23	15.8	44.2	1184	1.2	.09
S.D.	.290	.53	1.46	202.1	.78	.064
GROUP: 4 DOSE LEVEL: 800 DOSAGE UNIT: MG/KG						
08502	8.34	15.8	44.0	1070	1.9	.16
08503	7.79	14.4	40.4	1164	1.9	.15
08504	7.84	15.8	41.9	1376	2.0	.16
08506	7.53	14.0	38.0	1234	1.3	.10
08507	7.83	15.3	43.5	1047	2.2	.17
08508	8.05	15.1	42.2	1145	.7	.06
08509	7.91	15.4	42.8	1175	.7	.06
08510	8.61	16.3	45.3	972	.5	.04
08511	8.58	16.6	45.7	1289	.8	.07
08512	8.36	15.8	43.8	1167	.3	.03
MEAN	8.08	15.4	42.8	1164	1.2	.10
S.D.	.367	.80	2.30	118.0	.71	.055

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL (%)	MET TH/UL (%)	BAND TH/UL (%)	SEG TH/UL (%)	LYMPH TH/UL (%)	MONO TH/UL (%)	EOSIN TH/UL (%)	BASO TH/UL (%)
GROUP: 1	DOSE LEVEL: 0 DOSAGE UNIT: MG/KG								
08382	11.1	.0(0)	.0(0)	.0(0)	1.0(9)	9.9(89)	.1(1)	.1(1)	.0(0)
08383	10.8	.0(0)	.0(0)	.0(0)	2.5(23)	8.0(74)	.1(1)	.2(2)	.0(0)
08384	15.6	.0(0)	.0(0)	.0(0)	2.7(17)	12.3(79)	.3(2)	.3(2)	.0(0)
08385	9.7	.0(0)	.0(0)	.0(0)	2.1(22)	7.5(77)	.0(0)	.1(1)	.0(0)
08386	9.9	.0(0)	.0(0)	.0(0)	2.2(22)	7.5(76)	.0(0)	.2(2)	.0(0)
08387	13.7	.0(0)	.0(0)	.0(0)	1.0(7)	12.6(92)	.0(0)	.1(1)	.0(0)
08388	11.5	.0(0)	.0(0)	.0(0)	2.1(18)	9.3(81)	.1(1)	.0(0)	.0(0)
08389	12.3	.0(0)	.0(0)	.0(0)	1.2(10)	10.9(89)	.0(0)	.1(1)	.0(0)
08390	11.8	.0(0)	.0(0)	.0(0)	.8(7)	10.6(90)	.0(0)	.4(3)	.0(0)
08391	12.0	.0(0)	.0(0)	.0(0)	2.8(23)	9.2(77)	.0(0)	.0(0)	.0(0)
MEAN	11.8	.0	.0	.0	1.8	9.8	.1	.1	.0
S.D.	1.76	.00	.00	.00	.76	1.84	.10	.13	.00
GROUP: 2	DOSE LEVEL: 100 DOSAGE UNIT: MG/KG								
08422	12.6	.0(0)	.0(0)	.0(0)	1.8(14)	10.7(85)	.0(0)	.1(1)	.0(0)
08423	12.8	.0(0)	.0(0)	.0(0)	.8(6)	11.5(90)	.0(0)	.5(4)	.0(0)
08424	15.9	.0(0)	.0(0)	.0(0)	3.8(24)	11.1(70)	.3(2)	.6(4)	.0(0)
08425	9.5	.0(0)	.0(0)	.0(0)	2.9(31)	6.6(69)	.0(0)	.0(0)	.0(0)
08426	13.1	.0(0)	.0(0)	.0(0)	2.8(21)	10.1(77)	.3(2)	.0(0)	.0(0)
08427	17.1	.0(0)	.0(0)	.0(0)	1.9(11)	14.7(86)	.0(0)	.5(3)	.0(0)
08428	11.5	.0(0)	.0(0)	.0(0)	1.0(9)	9.7(84)	.0(0)	.8(7)	.0(0)
08429	12.1	.0(0)	.0(0)	.1(1)	2.2(18)	9.4(78)	.0(0)	.4(3)	.0(0)
08430	8.2	.0(0)	.0(0)	.0(0)	.7(8)	7.5(91)	.0(0)	.1(1)	.0(0)
08431	13.2	.0(0)	.0(0)	.0(0)	2.8(21)	10.3(78)	.0(0)	.1(1)	.0(0)
MEAN	12.6	.0	.0	.0	2.1	10.2	.1	.3	.0
S.D.	2.63	.00	.00	.03	1.03	2.21	.13	.28	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	MET TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)
GROUP: 3	DOSE LEVEL: 200								
	DOSAGE UNIT: MG/KG								
08462	7.9	.0(0)	.0(0)	.0(0)	.5(6)	7.3(92)	.0(0)	.2(2)	.0(0)
08463	10.5	.0(0)	.0(0)	.0(0)	.6(6)	9.7(92)	.1(1)	.1(1)	.0(0)
08464	11.3	.0(0)	.0(0)	.0(0)	2.3(20)	8.9(79)	.0(0)	.1(1)	.0(0)
08465	9.3	.0(0)	.0(0)	.0(0)	.7(8)	8.5(91)	.1(1)	.0(0)	.0(0)
08466	16.9	.0(0)	.0(0)	.0(0)	3.2(19)	13.0(77)	.2(1)	.5(3)	.0(0)
08467	13.4	.0(0)	.0(0)	.0(0)	1.7(13)	11.5(86)	.0(0)	.1(1)	.0(0)
08469	8.0	.0(0)	.0(0)	.0(0)	.3(4)	7.6(95)	.0(0)	.1(1)	.0(0)
08470	14.5	.0(0)	.0(0)	.0(0)	1.7(12)	12.6(87)	.0(0)	.1(1)	.0(0)
08471	18.1	.0(0)	.0(0)	.0(0)	1.8(10)	16.1(89)	.0(0)	.2(1)	.0(0)
08472	12.9	.0(0)	.0(0)	.0(0)	3.1(24)	9.8(76)	.0(0)	.0(0)	.0(0)
MEAN	12.3	.0	.0	.0	1.6	10.5	.0	.1	.0
S.D.	3.53	.00	.00	.00	1.06	2.78	.07	.14	.00
GROUP: 4	DOSE LEVEL: 800								
	DOSAGE UNIT: MG/KG								
08502	11.9	.0(0)	.0(0)	.0(0)	2.1(18)	9.4(79)	.2(2)	.1(1)	.0(0)
08503	8.2	.0(0)	.0(0)	.0(0)	2.2(27)	5.7(70)	.1(1)	.2(2)	.0(0)
08504	17.2	.0(0)	.0(0)	.0(0)	3.1(18)	13.9(81)	.0(0)	.2(1)	.0(0)
08506	15.9	.0(0)	.0(0)	.0(0)	5.9(37)	9.4(59)	.5(3)	.2(1)	.0(0)
08507	14.6	.0(0)	.0(0)	.0(0)	5.4(37)	8.9(61)	.1(1)	.1(1)	.0(0)
08508	11.8	.0(0)	.0(0)	.0(0)	2.6(22)	9.1(77)	.0(0)	.1(1)	.0(0)
08509	14.3	.0(0)	.0(0)	.0(0)	1.1(8)	12.9(90)	.0(0)	.3(2)	.0(0)
08510	11.4	.0(0)	.0(0)	.0(0)	1.1(10)	9.9(87)	.0(0)	.3(3)	.0(0)
08511	19.6	.0(0)	.0(0)	.0(0)	1.8(9)	17.6(90)	.0(0)	.2(1)	.0(0)
08512	11.7	.0(0)	.0(0)	.0(0)	1.3(11)	10.1(86)	.0(0)	.4(3)	.0(0)
MEAN	13.7	.0	.0	.0	2.7	10.7	.1	.2	.0
S.D.	3.32	.00	.00	.00	1.71	3.30	.16	.10	.00

HLA 2399108

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	POIK

GROUP: 1	DOSE LEVEL: 0		DOSAGE UNIT: MG/KG		
08382	T	-	T	-	-
08383	T	-	T	-	-
08384	T	-	T	-	-
08385	T	-	T	-	-
08386	T	-	T	-	-
08387	T	-	T	-	-
08388	T	-	T	-	-
08389	T	-	T	-	-
08390	T	-	T	-	-
08391	T	-	T	-	-
GROUP: 2	DOSE LEVEL: 100		DOSAGE UNIT: MG/KG		
08422	1+	-	T	-	-
08423	1+	-	1+	-	-
08424	T	-	T	-	-
08425	T	-	T	-	-
08426	T	-	T	-	-
08427	T	-	T	-	-
08428	T	-	T	-	-
08429	T	-	T	-	T
08430	T	-	T	-	-
08431	T	-	T	-	-
GROUP: 3	DOSE LEVEL: 200		DOSAGE UNIT: MG/KG		
08462	T	-	T	-	-
08463	T	-	T	-	-
08464	T	-	T	-	-
08465	T	-	T	-	-
08466	T	-	T	-	-
08467	T	-	T	-	-
08469	T	-	T	-	T
08470	T	-	T	-	-
08471	T	-	T	-	-
08472	T	-	T	-	-

HLA 2399108

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	POIK

GROUP: 4	DOSE LEVEL: 800		DOSAGE UNIT: MG/KG		
08502	T	-	T	-	-
08503	T	-	1+	-	-
08504	T	-	1+	-	-
08506	T	-	T	-	-
08507	T	-	T	-	-
08508	T	-	T	-	-
08509	T	-	T	-	-
08510	T	-	T	-	-
08511	T	-	T	-	-
08512	T	-	-	-	-



HAZLETON

LABORATORIES AMERICA, INC.
1330 - B PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

HLA 2399-108

- 141 -

APPENDIX 7

Individual Clinical Chemistry Values



HAZLETON

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- 142 -

KEY TO CLINICAL CHEMISTRY

H1 = Trace Hemolysis

H2 = Slight Hemolysis

H3 = Moderate Hemolysis

H4 = Marked Hemolysis

H5 = Severe Hemolysis

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 5	DOSE LEVEL: BASELINE							
	DOSAGE UNIT:							
08522 H1	23	1.0	125	54	196	41	295	671
08523	13	.6	88	69	72	24	186	279
08524	12	.6	82	78	62	28	180	220
08525	14	.6	96	60	83	21	143	607
08526	12	.6	70	81	65	25	203	81
MEAN	15	.7	92	68	96	28	201	372
S.D.	4.7	.18	20.6	11.5	56.7	7.8	56.7	255.5

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 5	DOSE LEVEL: BASELINE DOSAGE UNIT:									
08522H1	149.6	6.86	107.3	6.3	4.3	2.0	2.15	10.8	13.5	.1
08523	144.7	6.32	101.4	5.2	3.5	1.7	2.06	9.7	10.2	.0
08524	144.4	6.34	103.0	5.8	3.7	2.1	1.76	10.2	11.8	.1
08525	145.4	6.97	104.2	5.9	4.0	1.9	2.11	10.6	12.3	.2
08526	145.2	6.57	101.1	5.6	3.7	1.9	1.95	10.5	11.4	.2
MEAN	145.9	6.61	103.4	5.8	3.8	1.9	2.01	10.4	11.8	.1
S.D.	2.13	.296	2.51	.40	.31	.15	.157	.43	1.21	.08

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 1	DOSE LEVEL: 0			DOSAGE UNIT: MG/KG						
08362 H2	151.0	5.49	103.4	6.5	4.3	2.2	1.95	10.3	8.5	.1
08363	147.1	5.90	109.6	5.7	3.8	1.9	2.00	9.3	7.7	.1
08364	147.9	6.27	105.0	6.0	3.8	2.2	1.73	9.8	9.1	.1
08365 H1	147.2	6.46	105.8	5.9	3.8	2.1	1.81	10.0	10.2	.1
08366 H1	148.9	4.85	107.7	6.5	4.1	2.4	1.71	9.9	7.5	.2
08367 H1	148.9	6.71	107.7	6.5	4.0	2.5	1.60	10.5	10.7	.1
08368	146.1	6.12	102.6	5.7	3.7	2.0	1.85	10.1	8.3	.1
08369	145.8	6.20	100.5	5.8	3.7	2.1	1.76	10.2	9.4	.0
08370	148.8	6.06	100.1	5.8	3.8	2.0	1.90	10.0	8.5	.1
08371	148.8	6.07	102.5	5.6	3.5	2.1	1.67	10.2	9.0	.1
MEAN	148.0	6.01	104.5	6.0	3.8	2.1	1.80	10.0	8.9	.1
S.D.	1.56	.521	3.21	.36	.23	.18	.128	.33	1.02	.05
GROUP: 2	DOSE LEVEL: 100			DOSAGE UNIT: MG/KG						
08403	146.2	6.05	108.0	5.9	3.8	2.1	1.81	9.3	8.5	.0
08404 H1	147.1	6.60	108.8	6.4	4.0	2.4	1.67	9.7	7.6	.0
08405	148.8	6.20	106.6	6.0	4.1	1.9	2.16	9.9	10.0	.1
08406 H1	145.1	6.33	104.9	6.1	4.3	1.8	2.39	10.0	8.5	.1
08407	148.5	6.09	105.7	5.9	4.0	1.9	2.11	10.4	8.9	.0
08408 H1	147.0	6.36	102.8	6.4	3.9	2.5	1.56	10.2	8.6	.1
08409	145.0	6.36	105.0	5.8	3.8	2.0	1.90	10.1	9.1	.0
08410	147.7	6.51	100.8	6.1	4.2	1.9	2.21	10.8	9.5	.0
08411	145.5	6.05	101.1	6.0	3.6	2.4	1.90	10.4	8.8	.0
08412	146.4	6.51	102.8	6.1	3.8	2.3	1.65	10.2	9.0	.2
MEAN	146.7	6.31	104.6	6.1	3.9	2.1	1.90	10.1	8.8	.0
S.D.	1.34	.201	2.74	.20	.21	.26	.307	.41	.64	.07

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 3	DOSE LEVEL: 200									
	DOSAGE UNIT: MG/KG									
08442	147.1	5.85	103.8	6.2	4.0	2.2	1.82	9.4	7.7	.0
08443	148.2	6.10	107.4	5.9	4.0	1.9	2.11	9.8	8.3	.1
08444	148.8	6.57	100.8	6.2	3.9	2.3	1.70	10.2	9.5	.0
08445	149.7	5.86	104.1	6.0	3.9	2.1	1.86	9.9	7.8	.1
08447 H1	148.4	6.40	107.5	5.7	3.9	1.8	2.17	10.1	9.5	.0
08448	147.4	6.83	102.0	5.8	3.7	2.1	1.76	10.5	10.3	.1
08449	146.4	6.47	102.8	5.8	3.6	2.2	1.64	10.4	9.2	.0
08450	146.0	6.69	103.4	6.2	3.8	2.4	1.58	10.4	8.8	.1
08451	146.3	6.47	103.4	5.7	3.7	2.0	1.85	10.3	9.4	.0
08452	144.7	6.50	105.2	6.0	3.7	2.3	1.61	10.0	9.0	.1
MEAN	147.3	6.37	104.0	5.9	3.8	2.1	1.81	10.1	8.9	.0
S.D.	1.50	.333	2.15	.20	.14	.19	.200	.34	.82	.05
GROUP: 4	DOSE LEVEL: 800									
	DOSAGE UNIT: MG/KG									
08482	147.2	6.57	109.1	5.7	3.9	1.8	2.17	9.8	9.3	.0
08483	148.9	6.13	108.8	5.8	3.7	2.1	1.76	9.9	8.0	.0
08484 H1	148.8	6.62	106.1	6.1	4.0	2.1	1.90	9.9	9.9	.0
08485	147.9	6.52	104.4	6.0	4.1	1.9	2.16	10.2	8.7	.1
08486 H2	148.8	6.65	103.2	5.8	3.9	1.9	2.05	9.9	8.0	.1
08487 H1	144.8	6.03	106.1	5.7	3.6	2.1	1.71	10.2	10.4	.0
08488	146.2	6.27	102.8	6.0	3.4	2.6	1.31	10.4	8.5	.0
08489	148.7	7.03	105.5	5.8	3.9	1.9	2.05	9.8	10.1	.1
08490	147.9	6.88	99.8	6.0	3.9	2.1	1.86	10.3	9.0	.0
08491	147.0	6.87	104.1	6.1	3.8	2.3	1.65	10.3	9.6	.0
MEAN	147.6	6.56	105.0	5.9	3.8	2.1	1.86	10.1	9.1	.0
S.D.	1.34	.330	2.79	.16	.20	.23	.266	.23	.85	.05

APPENDIX 7
INDIVIDUAL CRITICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG								
08362 H1	12	.9	94	53	83	28	206	154
08363	16	.6	83	47	82	22	106	538
08364	17	.7	74	69	82	28	167	431
08365 H1	16	.6	94	64	95	30	119	492
08366 H1	14	.6	101	54	NO TEST ^a	NO TEST ^b	172	NO TEST ^c
08367 H1	10	.7	77	54	122	39	179	727
08368	11	.6	92	60	74	28	68	241
08369	10	.7	88	56	69	19	104	261
08370	10	.8	81	69	62	24	170	263
08371	13	.7	84	89	63	23	110	181
MEAN	13	.7	87	62	313	214	140	1219
S.D.	2.7	.10	8.5	12.0	733.4	592.4	44.1	2705.0
GROUP: 2 DOSE LEVEL: 100 DOSAGE UNIT: MG/KG								
08403	12	.7	85	35	81	28	117	729
08404 H1	17	.6	91	55	78	24	107	630
08405	15	.7	89	38	80	20	131	356
08406 H1	16	.6	90	73	81	24	76	546
08407	12	.5	82	58	70	21	114	225
08408 H1	11	.6	82	63	81	29	112	711
08409	10	.5	99	35	81	22	135	646
08410	12	.6	96	67	86	25	122	417
08411	12	.7	90	71	63	26	133	152
08412	11	.7	87	63	66	24	118	248
MEAN	13	.6	89	56	77	24	117	466
S.D.	2.3	.08	5.5	14.7	7.6	2.9	17.0	214.4

^a Deleted from statistics (individual value was 2400; mean and s.d. would have been 313 ± 733.4).

^b Deleted from statistics (individual value was 1900; mean and s.d. would have been 214 ± 592.4).

^c Deleted from statistics (individual value was 8900; mean and s.d. would have been 1219 ± 2705.0).

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 3	DOSE LEVEL: 200			DOSAGE UNIT: MG/KG				
08442	15	.7	89	61	78	29	144	402
08443	14	.7	121	61	67	27	132	309
08444	15	.7	89	45	76	22	124	211
08445	14	.7	84	50	68	23	86	121
08447H1	14	.5	94	50	84	22	103	430
08448	12	.7	98	42	82	25	146	782
08449	11	.6	79	62	73	32	118	276
08450	11	.7	80	71	90	37	199	236
08451	10	.8	80	47	57	24	191	230
08452	10	.7	101	65	69	23	120	527
MEAN	13	.7	92	55	74	26	136	352
S.D.	2.0	.08	12.9	9.8	9.7	4.9	35.7	192.4
GROUP: 4	DOSE LEVEL: 800			DOSAGE UNIT: MG/KG				
08482	12	.6	92	58	87	26	90	418
08483	11	.6	90	62	55	21	92	214
08484H1	14	.6	81	64	92	29	106	328
08485	15	.6	90	77	70	27	110	463
08486H1	12	.5	96	57	58	33	105	167
08487H1	13	.7	85	78	103	33	107	723
08488	27	.8	75	64	74	23	96	189
08489	15	.7	84	54	107	35	118	630
08490	6	.7	104	78	51	19	106	102
08491	12	.7	87	78	95	31	121	506
MEAN	14	.6	88	67	79	28	105	374
S.D.	5.3	.08	8.1	9.8	20.4	5.5	10.2	209.1

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 1	DOSE LEVEL: 0			DOSAGE UNIT: MG/KG						
08362	143.8	5.25	102.5	6.6	3.7	2.9	1.28	10.7	8.1	.2
08363	146.8	6.36	105.7	6.0	3.6	2.4	1.50	10.2	7.7	.2
08364	143.9	5.71	103.0	5.9	3.5	2.4	1.46	9.8	7.0	.2
08365H1	145.8	6.89	103.3	6.5	3.6	2.9	1.24	10.1	8.1	.2
08366	145.1	6.43	105.7	7.0	3.8	3.2	1.19	9.8	7.8	.0
08367	149.5	6.79	101.0	6.6	3.6	3.0	1.20	8.5	9.9	.2
08368	146.8	6.91	105.7	6.4	3.9	2.5	1.56	9.4	9.5	.2
08369	144.1	6.27	104.8	6.3	3.9	2.4	1.63	9.8	8.7	.2
08370	147.9	6.19	103.1	6.2	3.9	2.3	1.70	9.3	9.6	.2
08371	147.4	5.74	107.7	5.9	3.6	2.3	1.57	8.9	9.4	.2
MEAN	146.1	6.25	104.3	6.3	3.7	2.6	1.43	9.6	8.6	.2
S.D.	1.91	.551	2.00	.35	.15	.33	.190	.65	.98	.06
GROUP: 2	DOSE LEVEL: 100			DOSAGE UNIT: MG/KG						
08403	144.8	6.10	102.5	6.3	3.8	2.5	1.52	9.6	6.8	.2
08404	146.0	6.30	102.0	6.4	3.8	2.6	1.46	9.9	6.5	.1
08405	142.2	6.26	102.5	6.2	3.4	2.8	1.21	9.8	8.3	.1
08406	143.4	6.01	104.7	6.6	4.0	2.6	1.54	10.1	7.7	.3
08407	147.6	6.14	100.6	6.5	3.7	2.8	1.32	10.5	7.2	.2
08408	147.9	6.39	105.1	6.7	4.1	2.6	1.58	9.5	7.7	.2
08409	147.9	6.67	104.6	6.3	3.9	2.4	1.63	9.7	9.0	.2
08410	146.5	6.50	103.5	6.5	3.9	2.6	1.50	9.3	9.7	.2
08411	146.8	6.15	104.8	6.7	3.8	2.9	1.31	10.3	9.3	.2
08412	147.1	6.45	106.4	6.4	3.8	2.6	1.46	9.3	10.1	.2
MEAN	146.0	6.30	103.7	6.5	3.8	2.6	1.45	9.8	8.2	.2
S.D.	1.96	.206	1.75	.17	.19	.15	.133	.41	1.25	.06

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 3	DOSE LEVEL: 200									
	DOSAGE UNIT: MG/KG									
08442	145.0	6.08	103.3	6.3	3.8	2.5	1.52	9.7	6.9	.2
08443	146.3	6.61	103.7	6.4	3.9	2.5	1.56	10.7	7.7	.2
08444	143.8	5.98	98.7	6.2	3.5	2.7	1.30	10.1	7.9	.2
08445	143.2	5.98	99.8	6.5	3.6	2.9	1.24	9.8	5.7	.2
08447	145.8	5.76	104.2	6.4	3.7	2.7	1.37	10.2	7.2	.0
08449	143.5	6.00	106.0	6.5	3.9	2.6	1.50	8.7	8.2	.2
08451	145.9	5.93	106.2	6.2	3.8	2.4	1.58	10.0	9.7	.2
08452	148.3	6.76	108.5	6.4	3.8	2.6	1.46	9.8	8.7	.2
08453	145.8	6.43	107.5	6.2	3.6	2.6	1.38	9.4	9.3	.2
08455	147.3	6.27	104.9	6.4	3.8	2.6	1.46	9.0	10.1	.0
MEAN	145.5	6.18	104.3	6.3	3.7	2.6	1.44	9.7	8.1	.2
S.D.	1.65	.325	3.12	.12	.13	.14	.112	.59	1.36	.08
GROUP: 4	DOSE LEVEL: 800									
	DOSAGE UNIT: MG/KG									
08482	146.4	6.49	101.7	6.6	4.0	2.6	1.54	10.6	7.5	.1
08483	146.0	6.50	105.5	5.8	3.5	2.3	1.52	9.9	8.0	.1
08484	142.7	6.57	101.9	5.9	3.6	2.3	1.57	10.3	9.9	.1
08485	144.4	6.85	103.7	6.0	3.7	2.3	1.61	10.4	7.7	.2
08486	145.2	6.79	103.7	6.5	3.8	2.7	1.41	9.8	8.1	.2
08487 H1	146.8	6.51	109.2	6.6	4.1	2.5	1.64	9.5	10.1	.2
08488	145.4	6.57	105.9	5.9	3.0	2.9	1.03	9.0	10.6	.2
08489	148.1	6.77	108.3	6.4	4.2	2.2	1.91	9.1	9.9	.2
08490	147.2	6.56	103.1	6.2	3.9	2.3	1.70	9.8	8.9	.1
08492	147.4	6.17	104.0	6.2	3.9	2.3	1.70	9.1	10.8	.2
MEAN	146.0	6.58	104.7	6.2	3.8	2.4	1.56	9.7	9.1	.2
S.D.	1.60	.195	2.52	.30	.35	.23	.230	.57	1.25	.05

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 1	DOSE LEVEL: 0	DOSAGE UNIT: MG/KG						
08362	12	.7	100	64	76	23	136	313
08363	12	.6	103	64	65	25	70	172
08364	16	.7	105	90	57	22	90	133
08365 H1	12	.6	123	117	64	25	67	193
08366	18	.6	98	60	77	28	87	524
08367	9	.7	84	62	73	28	56	137
08368	13	.6	109	88	57	21	35	131
08369	13	.7	112	88	51	16	43	219
08370	9	.5	90	98	54	27	77	121
08371	12	.5	104	108	56	24	75	207
MEAN	13	.6	103	84	63	24	74	215
S.D.	2.8	.08	11.0	20.5	9.5	3.7	28.2	123.0
GROUP: 2	DOSE LEVEL: 100	DOSAGE UNIT: MG/KG						
08403	12	.6	109	49	57	29	91	221
08404	13	.6	109	68	43	21	65	111
08405	12	.6	112	45	60	20	90	259
08406	13	.6	123	109	74	23	50	510
08407	13	.6	110	81	50	16	76	111
08408	10	.6	96	88	71	24	97	556
08409	9	.5	110	42	56	18	91	196
08410	10	.5	105	93	55	16	83	289
08411	10	.5	108	109	47	19	86	109
08412	13	.5	103	80	64	24	73	143
MEAN	12	.6	109	76	58	21	80	251
S.D.	1.6	.05	6.9	24.9	9.9	4.1	14.4	162.1

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 3	DOSE LEVEL: 200			DOSAGE UNIT: MG/KG				
08442	14	.7	103	82	68	22	86	302
08443	15	.6	135	93	113	47	95	425
08444	15	.7	96	70	63	19	74	164
08445	14	.7	101	76	62	24	49	102
08447	16	.5	96	79	76	22	60	320
08449	13	.6	95	74	85	28	54	605
08451	11	.6	94	59	52	18	74	205
08452	14	.6	96	78	47	20	49	222
08453	12	.6	112	87	50	39	79	221
08455	11	.6	95	61	51	22	71	117
MEAN	14	.6	102	76	67	26	69	268
S.D.	1.7	.06	12.7	10.6	20.4	9.5	15.7	153.3
GROUP: 4	DOSE LEVEL: 800			DOSAGE UNIT: MG/KG				
08482	10	.5	108	93	71	32	62	175
08483	13	.6	93	63	63	23	91	300
08484	13	.6	103	72	55	24	60	142
08485	14	.6	99	86	80	45	123	413
08486	12	.5	95	75	75	38	69	393
08487 HI	14	.7	78	83	94	48	117	389
08488	23	.7	90	51	52	25	118	85
08489	11	.6	101	65	61	31	82	111
08490	7	.5	132	88	41	26	75	71
08492	11	.5	102	60	67	35	97	121
MEAN	13	.6	100	74	66	33	89	220
S.D.	4.2	.08	14.0	13.8	15.1	8.8	23.7	138.4

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 5	DOSE LEVEL: BASELINE							
	DOSAGE UNIT:							
08527 H1	17	.7	96	85	133	30	216	680
08528	13	.6	85	61	85	21	156	537
08529	17	.6	91	78	96	27	140	655
08530	13	.8	87	125	85	23	135	576
08531	13	.8	87	75	110	28	179	454
MEAN	15	.7	89	85	102	26	165	580
S.D.	2.2	.10	4.4	24.1	20.2	3.7	33.2	91.3

APPENDIX 7
 INDIVIDUAL CLINICAL CHEMISTRY VALUES
 SUBCHRONIC TOXICITY STUDY IN RATS
 WEEK -1 FEMALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 5	DOSE LEVEL: BASELINE									
	DOSAGE UNIT:									
08527H1	147.3	6.67	106.9	5.7	4.0	1.7	2.35	11.2	14.1	.2
08528	143.2	5.76	105.4	5.5	3.8	1.7	2.24	10.2	11.0	.1
08529	146.6	6.69	108.0	5.8	3.9	1.9	2.05	10.5	11.7	.8
08530	145.1	6.77	106.6	6.1	4.2	1.9	2.21	11.3	11.4	.1
08531	145.4	6.73	106.8	5.9	4.0	1.9	2.11	10.4	12.0	.0
MEAN	145.5	6.52	106.7	5.8	4.0	1.8	2.19	10.7	12.0	.1
S.D.	1.57	.429	.93	.22	.15	.11	.117	.50	1.21	.08

APPENDIX 7
INDIVIDUAL CHEMICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 3	DOSE LEVEL: 200									
	DOSAGE UNIT: MG/KG									
08462	142.8	5.61	107.9	6.4	4.3	2.1	2.05	10.0	8.0	.1
08463 HI	146.9	6.15	111.4	6.4	4.4	2.0	2.20	10.3	8.3	.1
08464 HI	146.7	6.90	107.2	5.8	4.1	1.7	2.41	9.8	10.4	.0
08465	148.0	6.19	108.2	6.6	4.4	2.2	2.00	10.4	8.7	.1
08466	147.3	6.37	112.4	6.1	4.1	2.0	2.05	10.1	8.9	.0
08467	144.2	5.72	106.0	6.6	4.4	2.2	2.00	10.7	7.3	.1
08469	143.0	6.09	104.3	6.1	3.8	2.3	1.65	10.4	8.3	.1
08470	145.8	6.10	104.7	6.1	3.8	2.3	1.65	10.5	8.3	.1
08471 HI	143.8	5.94	104.7	5.8	3.7	2.1	1.76	9.8	7.9	.0
08472	144.0	6.23	105.2	6.3	3.9	2.4	1.63	9.8	7.6	.0
MEAN	145.2	6.13	107.2	6.2	4.1	2.1	1.94	10.2	8.4	.1
S.D.	1.91	.356	2.84	.29	.28	.20	.262	.33	.86	.05
GROUP: 4	DOSE LEVEL: 800									
	DOSAGE UNIT: MG/KG									
08502	145.4	6.18	109.8	6.4	4.1	2.3	1.78	10.1	7.4	.0
08503	144.7	5.99	105.0	6.0	4.0	2.0	2.00	10.0	8.7	.0
08504	145.9	6.08	105.7	5.8	4.0	1.8	2.22	10.3	9.1	.0
08506	145.3	6.26	110.3	6.2	3.9	2.3	1.70	10.1	8.6	.1
08507	146.9	6.61	104.6	6.3	4.4	1.9	2.32	10.8	9.2	.0
08508	145.1	6.04	103.7	6.0	3.9	2.1	1.86	10.9	8.1	.1
08509 HI	141.4	5.62	106.4	6.0	4.1	1.9	2.16	10.3	9.6	.1
08510	145.9	6.63	102.3	5.9	3.9	2.0	1.95	10.8	8.1	.2
08511	146.5	6.00	101.6	6.6	4.2	2.4	1.75	10.6	8.2	.1
08512	146.6	6.15	103.9	6.4	3.8	2.6	1.46	10.2	7.8	.0
MEAN	145.4	6.16	105.3	6.2	4.0	2.1	1.92	10.4	8.5	.1
S.D.	1.56	.298	2.88	.26	.18	.26	.264	.33	.68	.07

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 1	DOSE LEVEL: 0									
	DOSAGE UNIT: MG/KG									
08382	143.2	5.44	109.6	6.0	4.0	2.0	2.00	9.6	6.9	.0
08383	145.9	5.48	108.5	6.3	4.2	2.1	2.00	9.6	6.2	.0
08384	148.2	6.20	110.0	6.7	5.0	1.7	2.94	10.7	9.7	.0
08385	146.4	5.64	107.9	6.4	4.1	2.3	1.78	10.0	7.7	.1
08386	149.5	5.60	106.5	6.0	4.1	1.9	2.16	9.8	7.7	.1
08387	143.1	5.24	102.8	6.3	4.1	2.2	1.86	10.1	8.2	.1
08388	144.0	5.74	102.2	5.9	4.2	1.7	2.47	10.3	7.2	.2
08389 HI	143.9	6.15	103.1	5.5	3.7	1.8	2.06	9.7	10.3	.1
08390	142.8	5.71	103.2	5.8	3.7	2.1	1.76	9.6	8.3	.2
08391	145.6	5.91	106.3	6.2	3.8	2.4	1.58	10.0	8.4	.0
MEAN	145.3	5.71	106.0	6.1	4.1	2.0	2.06	9.9	8.1	.1
S.D.	2.28	.305	2.98	.34	.37	.24	.394	.36	1.23	.08

GROUP: 2	DOSE LEVEL: 100									
	DOSAGE UNIT: MG/KG									
08422	144.9	5.55	109.3	5.9	4.0	1.9	2.11	9.5	6.1	.1
08423	146.5	6.03	110.1	6.3	4.1	2.2	1.86	10.2	8.1	.1
08424	146.9	6.59	106.8	6.3	4.2	2.1	2.00	10.0	8.9	.1
08425	145.4	6.16	108.0	7.1	4.7	2.4	1.96	10.7	8.8	.0
08426	147.8	6.40	107.5	5.5	4.0	1.5	2.67	10.0	9.8	.0
08427 HI	141.3	6.16	104.4	5.7	3.7	2.0	1.85	9.8	8.2	.0
08428	143.3	6.06	104.9	6.5	4.3	2.2	1.95	10.3	7.2	.2
08429	144.7	5.46	104.6	6.3	4.0	2.3	1.74	9.7	7.5	.0
08430	144.1	5.62	102.6	6.1	3.9	2.2	1.77	9.9	6.8	.0
08431	143.2	5.92	105.5	5.8	3.7	2.1	1.76	9.4	7.8	.0
MEAN	144.8	5.99	106.4	6.1	4.1	2.1	1.97	9.9	7.9	.0
S.D.	1.95	.366	2.37	.46	.30	.25	.274	.39	1.09	.07

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 1	DOSE LEVEL: 0	DOSAGE UNIT: MG/KG						
08382	17	.6	79	66	76	27	110	505
08383	18	.7	94	63	70	26	73	322
08384	14	.6	90	83	78	18	70	582
08385	16	.6	100	84	65	23	79	97
08386	16	.6	88	67	72	21	94	329
08387	14	.8	86	71	93	23	96	421
08388	22	.7	89	84	80	28	98	344
08389H1	13	.7	88	40	118	25	160	788
08390	13	.7	93	56	63	32	111	302
08391	13	.8	88	85	70	24	117	330
MEAN	16	.7	90	70	79	25	101	402
S.D.	2.9	.08	5.5	14.7	16.3	3.9	26.3	187.3
GROUP: 2	DOSE LEVEL: 100	DOSAGE UNIT: MG/KG						
08422	17	.7	83	70	106	43	144	509
08423	14	.6	98	83	80	21	102	402
08424	18	.8	82	78	92	30	108	491
08425	17	.7	94	59	84	21	107	234
08426	16	.7	82	58	90	25	87	533
08427H1	14	.6	93	68	73	28	60	441
08428	21	.6	97	59	80	38	78	268
08429	9	.8	99	74	93	25	201	430
08430	15	.7	84	95	63	23	61	215
08431	14	.7	94	92	63	26	55	292
MEAN	16	.7	91	74	82	28	100	382
S.D.	3.2	.07	7.0	13.4	13.6	7.3	44.8	119.2

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 3	DOSE LEVEL: 200							
	DOSAGE UNIT: MG/KG							
08462	16	.7	80	91	85	24	111	771
08463 HI	17	.6	88	88	69	22	90	337
08464 HI	14	.7	85	51	83	22	94	513
08465	16	.7	84	76	71	20	104	338
08466	17	.7	84	86	73	24	92	331
08467	11	.7	99	99	85	20	119	381
08469	18	.7	102	74	56	23	69	223
08470	8	.8	77	81	74	31	88	461
08471 HI	8	.7	82	75	90	28	100	725
08472	8	.7	106	107	81	26	72	343
MEAN	13	.7	89	83	77	24	94	442
S.D.	4.1	.05	10.0	15.5	10.1	3.5	15.7	179.3
GROUP: 4	DOSE LEVEL: 800							
	DOSAGE UNIT: MG/KG							
08502	16	.6	85	103	80	30	83	379
08503	15	.6	86	74	75	20	51	695
08504	14	.7	87	88	70	26	84	272
08506	14	.6	78	95	75	25	50	457
08507	14	.6	87	100	73	23	114	180
08508	14	.7	82	104	65	24	87	294
08509 HI	19	.6	90	68	91	32	126	760
08510	9	.7	77	98	67	19	96	378
08511	10	.7	88	115	74	30	70	407
08512	14	.7	90	101	58	24	60	85
MEAN	14	.6	85	95	73	25	82	391
S.D.	2.8	.05	4.6	14.3	8.9	4.3	25.4	209.6

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 3	DOSE LEVEL: 200									
	DOSAGE UNIT: MG/KG									
08462	142.5	5.56	104.7	6.8	4.3	2.5	1.72	10.2	5.5	.2
08463	143.5	6.50	103.8	6.6	4.0	2.6	1.54	10.5	7.6	.2
08464	145.9	6.22	103.5	6.2	3.7	2.5	1.48	10.1	7.5	.2
08465	144.2	5.84	108.4	6.7	3.8	2.9	1.31	9.5	7.2	.0
08466	145.8	5.73	106.0	6.2	3.7	2.5	1.48	9.9	6.2	.1
08467	143.0	5.74	105.9	7.2	4.7	2.5	1.88	10.5	7.8	.3
08469	145.2	6.57	110.2	6.7	4.0	2.7	1.48	9.9	8.2	.2
08470	145.9	5.68	109.2	6.9	4.1	2.8	1.46	9.9	8.0	.2
08471	144.4	5.43	104.8	6.9	4.2	2.7	1.56	10.1	7.2	.2
08472	144.0	6.52	106.6	6.9	4.2	2.7	1.56	9.6	7.6	.2
MEAN	144.4	5.98	106.3	6.7	4.1	2.6	1.55	10.0	7.3	.2
S.D.	1.23	.432	2.29	.31	.31	.14	.156	.33	.83	.08
GROUP: 4	DOSE LEVEL: 800									
	DOSAGE UNIT: MG/KG									
08502	144.1	6.19	106.2	6.9	3.8	3.1	1.23	10.2	6.2	.1
08503	143.4	5.98	104.3	6.5	4.0	2.5	1.60	10.4	7.1	.1
08504	145.3	6.03	104.5	6.5	3.7	2.8	1.32	10.4	6.1	.2
08506	145.7	6.43	105.8	6.3	3.6	2.7	1.33	10.2	7.5	.1
08507	144.3	6.04	104.7	6.6	4.1	2.5	1.64	10.3	6.6	.2
08508	142.5	6.04	105.9	6.7	4.2	2.5	1.68	10.3	8.9	.2
08509	142.7	6.02	108.1	6.7	4.1	2.6	1.58	10.3	7.7	.2
08510	145.5	6.94	108.5	6.8	4.5	2.3	1.96	10.3	9.5	.2
08511	145.7	6.00	105.9	7.2	4.4	2.8	1.57	9.9	8.5	.2
08512	146.7	6.50	107.9	7.3	4.4	2.9	1.52	9.9	9.7	.2
MEAN	144.6	6.22	106.2	6.8	4.1	2.7	1.54	10.2	7.8	.2
S.D.	1.41	.314	1.52	.31	.31	.24	.211	.18	1.32	.05

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	SODIUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
GROUP: 1	DOSE LEVEL: 0			DOSAGE UNIT: MG/KG						
08382	143.4	5.75	104.2	6.5	4.2	2.3	1.83	10.3	5.8	.2
08383	143.4	5.82	106.5	6.6	3.9	2.7	1.44	9.7	4.6	.1
08384H1	145.7	6.32	103.0	6.2	3.8	2.4	1.58	9.8	7.1	.2
08385	142.2	5.81	106.2	6.6	3.9	2.7	1.44	9.7	5.5	.2
08386	145.2	5.85	106.8	6.8	4.0	2.8	1.43	9.8	5.9	.2
08387H1	143.9	6.53	108.1	7.1	4.6	2.5	1.84	10.1	9.8	.2
08388	144.9	6.18	107.3	6.8	4.4	2.4	1.83	10.0	7.5	.2
08389	145.1	6.56	104.8	7.0	4.3	2.7	1.59	9.3	9.3	.3
08390	144.2	6.84	108.1	6.4	3.9	2.5	1.56	9.8	7.9	.1
08391	146.6	5.90	104.9	7.0	4.1	2.9	1.41	9.4	10.3	.2
MEAN	144.5	6.16	106.0	6.7	4.1	2.6	1.59	9.8	7.4	.2
S.D.	1.29	.388	1.71	.29	.26	.20	.177	.30	1.95	.06
GROUP: 2	DOSE LEVEL: 100			DOSAGE UNIT: MG/KG						
08422H1	145.2	6.27	108.0	6.3	3.9	2.4	1.63	10.1	6.9	.2
08423H1	144.2	5.93	106.0	6.5	4.1	2.4	1.71	10.3	7.3	.1
08424H2	144.5	6.58	103.5	6.5	3.9	2.6	1.50	9.9	7.0	.3
08425	142.9	5.80	109.1	7.5	4.4	3.1	1.42	10.2	6.6	.2
08426	147.0	6.70	106.8	7.1	4.2	2.9	1.45	10.6	8.1	.2
08427H1	145.2	5.96	108.8	6.6	4.2	2.4	1.75	9.8	8.7	.2
08428	143.6	6.00	107.7	6.9	4.4	2.5	1.76	10.2	6.7	.2
08429	147.2	5.88	109.2	6.3	4.0	2.3	1.74	9.5	7.6	.1
08430	145.1	5.93	103.1	6.8	4.3	2.5	1.72	10.2	6.9	.2
08431	144.8	6.32	105.7	6.2	3.9	2.3	1.70	9.4	7.4	.2
MEAN	145.0	6.14	106.8	6.7	4.1	2.5	1.64	10.0	7.3	.2
S.D.	1.34	.313	2.20	.41	.20	.26	.131	.37	.66	.06

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG								
08382	15	.6	98	79	54	19	48	230
08383	15	.3	95	66	80	37	46	381
08384 H1	9	.7	95	114	65	21	46	241
08385	15	.6	97	109	67	24	54	104
08386	15	.6	88	90	72	18	40	394
08387 H1	16	.7	90	113	99	21	41	589
08388	15	.6	104	94	79	19	43	459
08389	14	.6	93	91	81	22	53	388
08390	14	.6	93	66	57	23	32	158
08391	15	.6	99	109	71	20	64	162
MEAN	14	.6	95	93	73	22	47	311
S.D.	1.9	.11	4.6	18.3	13.1	5.5	8.8	155.2
GROUP: 2 DOSE LEVEL: 100 DOSAGE UNIT: MG/KG								
08422 H1	14	.6	100	82	67	23	81	282
08423 H1	15	.7	104	85	68	21	52	364
08424 H2	16	.6	86	128	84	29	64	400
08425	16	.7	99	69	71	23	53	179
08426	14	.7	89	85	99	26	70	497
08427 H1	13	.6	109	118	59	29	60	140
08428	14	.6	101	87	82	38	47	285
08429	12	.7	105	78	76	19	96	280
08430	12	.4	99	122	53	20	29	57
08431	14	.6	92	124	51	18	29	129
MEAN	14	.6	98	98	71	25	58	261
S.D.	1.4	.09	7.3	22.4	14.9	6.1	21.1	136.4

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	ALK P U/L	LDH U/L
GROUP: 3	DOSE LEVEL: 200			DOSAGE UNIT: MG/KG				
08462	14	.6	90	126	58	20	65	225
08463	14	.6	94	115	55	16	41	217
08464	13	.6	89	67	65	22	70	207
08465	16	.7	77	91	73	24	61	332
08466	15	.7	159	123	70	22	46	106
08467	12	.6	110	113	64	24	78	236
08469	12	.6	94	105	64	27	46	153
08470	9	.6	82	93	64	27	44	305
08471	12	.6	92	129	80	29	52	295
08472	11	.6	111	131	66	24	41	155
MEAN	13	.6	100	109	66	24	54	223
S.D.	2.0	.04	23.4	20.5	7.1	3.8	13.2	72.6
GROUP: 4	DOSE LEVEL: 800			DOSAGE UNIT: MG/KG				
08502	15	.6	106	122	80	44	39	131
08503	14	.6	104	105	55	18	27	316
08504	11	.6	105	142	60	32	62	119
08506	15	.6	88	123	84	24	23	349
08507	14	.6	96	158	59	20	70	136
08508	15	.6	90	124	52	22	51	220
08509	15	.5	91	117	59	44	84	337
08510	10	.6	81	127	59	25	41	484
08511	11	.6	119	155	86	29	49	405
08512	18	.6	90	155	53	29	46	101
MEAN	14	.6	97	133	65	29	49	260
S.D.	2.4	.03	11.3	18.4	13.2	9.1	18.8	136.2



HAZLETON

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1330 - B PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

HLA 2399-108

- 163 -

APPENDIX 8

Individual Animal Summary Report

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 164

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08362 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 563.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 8:16 PROSECTOR: DOUGLAS HERNDON RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	O R G A N	
				S T A T U S	
ADRENAL (AD)	.046	.0082 %	.0206	WEIGHT TAKEN	
BRAIN W/STEM (BR)	2.23	.396 %	1.000	WEIGHT TAKEN	
HEART (HT)	1.65	.293 %	.740	WEIGHT TAKEN	
SPLEEN (SP)	.82	.146 %	.368	WEIGHT TAKEN	
KIDNEY (KD)	3.52	.625 %	1.578	WEIGHT TAKEN	
LIVER (LI)	13.84	2.457 %	6.206	WEIGHT TAKEN	
TESTIS/EPIDID (TP)	5.50	.977 %	2.466	WEIGHT TAKEN	

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 165

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808362 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 563.2 GRAMS
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PROSECTOR: DOUGLAS HERNDON PATHOLOGIST: SID JONES, DUM, PHD, DACUP RECORDER: SID JONES, DUM, PHD, DACUP
WEIGHER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV),
SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 166

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08763 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 452.7 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 10:53 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.062	.0137 %	.0297	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.10	.463 %	1.000	WEIGHT TAKEN
HEART (HT)	1.36	.301 %	.650	WEIGHT TAKEN
SPLEEN (SP)	.70	.155 %	.335	WEIGHT TAKEN
KIDNEY (KD)	2.88	.636 %	1.374	WEIGHT TAKEN
LIVER (LI)	11.04	2.439 %	5.268	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.92	1.086 %	2.345	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

EYE (EY) :
-CHRONIC INFLAMMATION, HARDERIAN GLAND, -SLIGHT
HEART (HT) :
-CARDIOMYOPATHY, DEGENERATIVE, -MINIMAL
LIVER (LI) :
-FOCAL HEPATITIS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08363 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 452.7 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 10:53 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU),
SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08364

SEX: MALE

DOSE GROUP: 1

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 95

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 543.3 GRAMS

DATE AND TIME OF NECROPSY: 07/14/86 13:21

PROSECTOR: DOUGLAS HERNDON

REORDER: SID JONES, DUM, PHD, DACUP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.051	.0094 %	.0244	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.10	.387 %	1.000	WEIGHT TAKEN
HEART (HT)	1.51	.278 %	.720	WEIGHT TAKEN
SPLEEN (SP)	1.07	.196 %	.507	WEIGHT TAKEN
KIDNEY (KD)	3.04	.559 %	1.445	WEIGHT TAKEN
LIVER (LI)	14.17	2.609 %	6.743	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.83	1.072 %	2.772	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	BONE, FEMUR (FE): -ARTICULAR SURFACE NOT PRESENT,-PRESENT HEART (HT): -CARDIOMYOPATHY, DEGENERATIVE,-MINIMAL LACRIMAL GL, EXO (EO): -FOCAL MONONUCLEAR INFILTRATE,-SLIGHT LUNG (LU): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 169

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08364 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 543.3 GRAMS
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PROSECTOR: DOUGLAS HERNDON PATHOLOGIST: SID JONES, DVM, PHD, DACUP RECORDER: SID JONES, DVM, PHD, DACUP
WEIGHER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
ESOPHAGUS (ES), EYE (EY), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08365 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 605.9 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 14:42 PROSECTOR: TIM GROVE RECORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.053	.0088 %	.0277	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.93	.318 %	1.000	WEIGHT TAKEN
HEART (HT)	1.50	.247 %	.777	WEIGHT TAKEN
SPLEEN (SP)	.80	.132 %	.414	WEIGHT TAKEN
KIDNEY (KD)	3.82	.631 %	1.983	WEIGHT TAKEN
LIVER (LI)	14.97	2.471 %	7.767	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.34	.881 %	2.770	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	ADRENAL, CORTEX (AC) : -VACUOLIZATION,-SLIGHT EYE (EY) : -CHRONIC INFLAMMATION, HARDERIAN GLAND,- MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT PANCREAS (PA) : -INFLAMMATION, CHRONIC,-SLIGHT

INDIVIDUAL ANIMAL SUMMARY REPORT STUDY NUMBER: 2399108

ANIMAL NUMBER: B08365 SEX: MALE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE AND TIME OF NECROPSY: 07/14/86 14:42 PROSECTOR: TIM GROVE REORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIOYIMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIOYIMIS (EP),
ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08366 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 457.0 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 15:07 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.067	.0147 %	.0329	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.05	.448 %	1.000	WEIGHT TAKEN
HEART (HT)	1.28	.279 %	.623	WEIGHT TAKEN
SPLEEN (SP)	.84	.184 %	.411	WEIGHT TAKEN
KIDNEY (KD)	3.28	.718 %	1.601	WEIGHT TAKEN
LIVER (LI)	12.41	2.716 %	6.058	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.17	1.130 %	2.521	WEIGHT TAKEN

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS
NECROPSY

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

ADRENAL, CORTEX (AC) :

-VACUOLIZATION,-SLIGHT

EYE (EY) :

-CHRONIC INFLAMMATION, HARDERIAN GLAND,-
SLIGHT

KIDNEY (KD) :

-NEPHROPATHY, CHRONIC PROGRESSIVE,-
SLIGHT

LIVER (LI) :

-BILE DUCT, INFLAMMATION, CHRONIC,-
MINIMAL

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

PARATHYROID (PT) :

>SECTION EXAMINED; TISSUE NOT PRESENT

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08366 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 457.0 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 15:07 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EG), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 174

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808367 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 451.7 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:10 PROSECTOR: DOUGLAS HERNDON
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-RIGHT EYE-CHROMODACRYORRHEA

NECROPSY

EYE (EY) :

-GLOBE RUPTURED POST MORTEM; LEFT
^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:RIGHT EYE-
CHROMODACRYORRHEA

HISTOPATHOLOGY

EYE (EY) :

>UNREMARKABLE
LIVER (LI) :
-BILE DUCT, INFLAMMATION, CHRONIC,-
MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08367 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 451.7 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:10 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.069	.0136 %	.0339	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.04	.399 %	1.000	WEIGHT TAKEN
HEART (HT)	1.41	.275 %	.690	WEIGHT TAKEN
SPLEEN (SP)	.62	.121 %	.302	WEIGHT TAKEN
KIDNEY (KD)	3.19	.624 %	1.562	WEIGHT TAKEN
LIVER (LI)	13.00	2.543 %	6.368	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.73	1.120 %	2.804	WEIGHT TAKEN

CLINICAL OBSERVATIONS	GENERAL INFORMATION (XX) :	EYE (EY) :	HISTOPATHOLOGY
-APPEARED NORMAL	>NOTE:>EXTERNAL OBSERVATIONS:NONE	-CHRONIC INFLAMMATION, HARDERIAN GLAND, -SLIGHT LUNG (LU) :	-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08368 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 511.3 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:08 PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08369

SEX: MALE

DOSE GROUP: 1

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/15/86

STUDY DAY OF DEATH: 96

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 508.4 GRAMS

DATE AND TIME OF NECROPSY: 07/15/86 10:00

PROSECTOR: TIM GROVE

REORDER: SID JONES, DUM, PHD, DACUP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.057	.0112 %	.0285	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.99	.392 %	1.000	WEIGHT TAKEN
HEART (HT)	1.17	.230 %	.586	WEIGHT TAKEN
SPLEEN (SP)	.81	.159 %	.405	WEIGHT TAKEN
KIDNEY (KD)	2.99	.588 %	1.499	WEIGHT TAKEN
LIVER (LI)	11.23	2.210 %	5.632	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.06	.996 %	2.538	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	NECROPSY GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	EYE (EY) : -CHRONIC INFLAMMATION, HARDERIAN GLAND, -SLIGHT HEART (HT) : -CARDIOMYOPATHY, DEGENERATIVE,-MINIMAL KIDNEY (KD) : -NEPHROPATHY, CHRONIC PROGRESSIVE,-MINIMAL LUNG (LU) : -TUBULE, MICROCONCRETION,-SLIGHT -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT MAMMARY GLAND (MG) : >SECTION EXAMINED; TISSUE NOT PRESENT PANCREAS (PA) : -INFLAMMATION, CHRONIC,-MINIMAL PARATHYROID (PT) : >SECTION EXAMINED; TISSUE NOT PRESENT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 179

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08369 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 508.4 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 10:00 PROSECTOR: TIM GROVE RECORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXD (EO), LIVER (LI),
LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN),
PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08370

SEX: MALE

DOSE GROUP: 1

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/15/86

STUDY DAY OF DEATH: 96

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 459.9 GRAMS

DATE AND TIME OF NECROPSY: 07/15/86 13:59

PROSECTOR: TIM GROVE

RECORDED: SID JONES, DUM, PHD, DACUP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.048	.0104 %	.0232	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.07	.451 %	1.000	WEIGHT TAKEN
HEART (HT)	1.29	.282 %	.625	WEIGHT TAKEN
SPLEEN (SP)	.63	.137 %	.303	WEIGHT TAKEN
KIDNEY (KD)	3.05	.664 %	1.474	WEIGHT TAKEN
LIVER (LI)	11.17	2.429 %	5.392	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.91	1.068 %	2.370	WEIGHT TAKEN

CLINICAL OBSERVATIONS

APPEARED NORMAL

PATHOLOGY OBSERVATIONS

NECROPSY

KIDNEY (KD):

-PELVIS, DILATED; LEFT, SLIGHTLY

-H-PELVIS, DILATED; RIGHT, SLIGHTLY.

GENERAL INFORMATION (XX):

>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

EYE (EY):

-ONE EXAMINED,-PRESENT

KIDNEY (KD):

-NEPHROPATHY, CHRONIC PROGRESSIVE,-MINIMAL

LUNG (LU):

-PELVIS, DILATATION,-SLIGHT

-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

PARATHYROID (PT):

>SECTION EXAMINED; TISSUE NOT PRESENT

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808370 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 459.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 13:59 PROSECTOR: TIM GROVE REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08371 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 493.7 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 15:13 PROSECTOR: TIM GROVE RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.051	.0103 %	.0264	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.93	.391 %	1.000	WEIGHT TAKEN
HEART (HT)	1.38	.280 %	.715	WEIGHT TAKEN
SPLEEN (SP)	1.17	.237 %	.606	WEIGHT TAKEN
KIDNEY (KD)	3.45	.699 %	1.788	WEIGHT TAKEN
LIVER (LI)	13.44	2.722 %	6.964	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.17	1.047 %	2.679	WEIGHT TAKEN

CLINICAL OBSERVATIONS

-LEFT EYE-CHROMODACRYORRHEA; MALOCCLUSION

PATHOLOGY OBSERVATIONS

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:LEFT EYE-CHROMODACRYORRHEA, MALOCCLUSION

HISTOPATHOLOGY

EYE (EY) :
-CHRONIC INFLAMMATION, HARDERIAN GLAND, -SLIGHT
HEART (HT) :
-CARDIOMYOPATHY, DEGENERATIVE, -MINIMAL
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
-BILE DUCT, INFLAMMATION, CHRONIC, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08371 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 493.7 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 15:13 PROSECTOR: TIM GROVE RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 184

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08372 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 487.8 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:32 PROSECTOR: DOUGLAS HERNDON RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE,-
MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08372 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 487.8 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:32 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 186

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808373 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 588.4 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 10:08 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS,-MINIMAL
-BILE DUCT, INFLAMMATION, CHRONIC,-
MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (ED), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08374 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 524.3 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 15:18 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	STATUS
ADRENAL (AD)	.048	.0092 %	.0240	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.00	.381 %	1.000	WEIGHT TAKEN
HEART (HT)	1.19	.227 %	.595	WEIGHT TAKEN
SPLEEN (SP)	1.04	.198 %	.520	WEIGHT TAKEN
KIDNEY (KD)	3.26	.622 %	1.630	WEIGHT TAKEN
LIVER (LI)	13.20	2.518 %	6.600	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.78	.912 %	2.390	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	HEART (HT) : -CARDIOMYOPATHY, DEGENERATIVE,-MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT PARATHYROID (PT) : >SECTION EXAMINED; TISSUE NOT PRESENT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 188

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808374 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 524.3 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 15:18 PROSECTOR: BARBARA DAY REORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE),
SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH),
THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08375 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 459.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:38 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
MAMMARY GLAND (MG) :
>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SO),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08376 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 518.8 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:47 PROSECTOR: TIM GROVE RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.056	.0108 %	.0279	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.01	.387 %	1.000	WEIGHT TAKEN
HEART (HT)	1.36	.262 %	.677	WEIGHT TAKEN
SPLEEN (SP)	.89	.172 %	.443	WEIGHT TAKEN
KIDNEY (KD)	3.21	.619 %	1.597	WEIGHT TAKEN
LIVER (LI)	14.85	2.862 %	7.388	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.23	1.008 %	2.602	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 191

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08376 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 518.8 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:47 PROSECTOR: TIM GROVE REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU),
TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 192

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08377 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 492.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:59 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LJ) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -MODERATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU),
TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808378 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 498.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:57 PROSECTOR: TIM GROVE RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.057	.0114 %	.0270	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.11	.424 %	1.000	WEIGHT TAKEN
HEART (HT)	1.33	.267 %	.630	WEIGHT TAKEN
SPLEEN (SP)	.76	.153 %	.360	WEIGHT TAKEN
KIDNEY (KD)	3.35	.673 %	1.588	WEIGHT TAKEN
LIVER (LI)	17.18	3.449 %	8.142	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.00	1.004 %	2.370	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	ADRENAL, CORTEX (AC) : -VACUOLIZATION,-SLIGHT LADRIMAL GL, EXD (ED) : -FOCAL MONONUCLEAR INFILTRATE,-MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT TESTIS (TE) : -DEGENERATION,-SLIGHT

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808378 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 498.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:57 PROSECTOR: TIM GROVE REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: TIM GROVE

STUDY NUMBER: 2399108

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LIVER (LI), LN, MESENTERIC (MS),
MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN),
PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08379 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 494.7 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:13 PROSECTOR: TIM GROVE RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP MEASURER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.050	.0101 %	.0249	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.01	.406 %	1.000	WEIGHT TAKEN
HEART (HT)	1.23	.249 %	.612	WEIGHT TAKEN
SPLEEN (SP)	.54	.109 %	.269	WEIGHT TAKEN
KIDNEY (KO)	2.85	.576 %	1.418	WEIGHT TAKEN
LIVER (LI)	12.80	2.587 %	6.368	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.48	.906 %	2.229	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	KIDNEY (KO) : -NEPHROPATHY, CHRONIC PROGRESSIVE, MINIMAL LIVER (LI) : -BILE DUCT, INFLAMMATION, CHRONIC, MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 196

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08379 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 494.7 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:13 PROSECTOR: TIM GROVE RECORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), NERVE, SCIATIC (SN), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYROID (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU),
SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08380		SEX: MALE		DOSE GROUP: 1		SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE	
DATE OF DEATH: 07/16/86		STUDY DAY OF DEATH: 97		STUDY WEEK OF DEATH: 14		TERMINAL BODY WEIGHT: 554.1 GRAMS	
DATE AND TIME OF NECROPSY: 07/16/86 14:44		PROSECTOR: TIM GROVE		PATHOLOGIST: SID JONES, DUM, PHD, DACUP		REORDER: SID JONES, DUM, PHD, DACUP	
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL		WEIGHER: TIM GROVE					
ORGAN NAME		ABSOLUTE ORGAN WEIGHT (GRAMS)		ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)		ORGAN TO BRAIN WEIGHT RATIO	
ADRENAL (AD)		.057		.0103 %		.0288	
BRAIN W/STEM (BR)		1.98		.357 %		1.000	
HEART (HT)		1.45		.262 %		.732	
SPLEEN (SP)		.93		.168 %		.470	
KIDNEY (KD)		3.65		.659 %		1.843	
LIVER (LI)		13.30		2.400 %		6.717	
TESTIS/EPIDID (TP)		5.06		.913 %		2.556	
CLINICAL OBSERVATIONS		P A T H O L O G Y O B S E R V A T I O N S					
-APPEARED NORMAL		GENERAL INFORMATION (XX) :		NECROPSY		HISTOPATHOLOGY	
		>NOTE:>EXTERNAL OBSERVATIONS:NONE				LUNG (LU) :	
						-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT PARATHYROID (PT) :	
						>SECTION EXAMINED; TISSUE NOT PRESENT	

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 198

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08380 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 554.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:44 PROSECTOR: TIM GROVE RECORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08381 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 479.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:52 PROSECTOR: BARBARA DAY REORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.059	.0123 %	.0272	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.17	.453 %	1.000	WEIGHT TAKEN
HEART (HT)	1.25	.261 %	.576	WEIGHT TAKEN
SPLEEN (SP)	.92	.192 %	.424	WEIGHT TAKEN
KIDNEY (KD)	2.70	.564 %	1.244	WEIGHT TAKEN
LIVER (LI)	9.99	2.086 %	4.604	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.25	1.096 %	2.419	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LACRIMAL GL, EXO (EO):
-FOCAL MONONUCLEAR INFILTRATE, -MINIMAL LUNG (LU):
-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT THYMUS (TH):
>TISSUE MISSING

APPENDIX 8

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 200

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808381 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 479.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:52 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACVP WEIGHER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE),
SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08402 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: UNSCHEDULED (M)
DATE OF DEATH: 04/23/86 STUDY WEEK OF DEATH: 2 TERMINAL BODY WEIGHT: 265.5 GRAMS
DATE AND TIME OF NECROPSY: 04/23/86 15:07 PROSECTOR: JAMES CANNON RECORDER: JAMES CANNON
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	P A T H O L O G Y O B S E R V A T I O N S	HISTOPATHOLOGY
-APPEARED NORMAL	NECROPSY LIVER (LI) : -H-ENLARGED LN, OTHER (LN) : -ENLARGED; MANDIBULAR SKIN, OTHER (SS) : -SORE; RIGHT LATERAL NECK, ONE, CRUSTY, OPEN, MARGINS NECROTIC, TAN TO DARK RED, 2.0 X 2.0 CM; LEFT LATERAL NECK, ONE, CRUSTY, OPEN, TAN TO DARK RED, 1.0 X 1.0 CM GENERAL INFORMATION (XX) : >NOTE:>REASON FOR SACRIFICE AND EXTERNAL OBSERVATIONS:NECK- NECROTIC SORES, SECTIONS IN JAR	BONE, FEMUR (FE) : -ARTICULAR SURFACE NOT PRESENT,-PRESENT LIVER (LI) : -FOCI OF MONONUCLEAR CELLS,-MINIMAL LN, OTHER (LN) : -HYPERPLASIA, LYMPHOID,-MODERATE MAMMARY GLAND (MG) : >SECTION EXAMINED; TISSUE NOT PRESENT SKIN, OTHER (SS) : -INFLAMMATION, GRANULOMATOUS,-SEVERE

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 202

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08402 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: UNSCHEDULED (M)
DATE OF DEATH: 04/23/86 STUDY DAY OF DEATH: 13 STUDY WEEK OF DEATH: 2 TERMINAL BODY WEIGHT: 265.5 GRAMS
DATE AND TIME OF NECROPSY: 04/23/86 15:07 PROSECTOR: JAMES CANNON REORDER: JAMES CANNON
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), LUNG (LU), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV),
SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08403 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 516.3 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:18 PROSECTOR: TIM GROVE RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

TESTIS (TE) :

-SOFT; RIGHT

-PALE; RIGHT, YELLOW

-CYST; RIGHT, FLUID FILLED

^COLLECTED/TAKEN (XW) :

-ELECTRON MICROSCOPY SAMPLE; LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,

INFILTRATION, LYMPHOID, -MINIMAL

TESTIS (TE) :

-DEGENERATION, -MODERATELY SEVERE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08404 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 512.3 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 8:45 PROSECTOR: TIM GROVE RECORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACVP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.044	.0086 %	.0208	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.12	.414 %	1.000	WEIGHT TAKEN
HEART (HT)	1.40	.273 %	.660	WEIGHT TAKEN
SPLEEN (SP)	.74	.144 %	.349	WEIGHT TAKEN
KIDNEY (KD)	3.31	.646 %	1.561	WEIGHT TAKEN
LIVER (LI)	14.75	2.879 %	6.958	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.46	1.066 %	2.575	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), *COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

***. ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT TO BODY WEIGHT (%)	RELATIVE WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	O R G A N	
					S T A T U S	
ADRENAL (AD)	.046	.0093 %		.0229	WEIGHT TAKEN	
BRAIN W/STEM (BR)	2.01	.407 %		1.000	WEIGHT TAKEN	
HEART (HT)	1.36	.277 %		.679	WEIGHT TAKEN	
SPLEEN (SP)	.89	.180 %		.442	WEIGHT TAKEN	
KIDNEY (KD)	3.23	.656 %		1.611	WEIGHT TAKEN	
LIVER (LI)	12.91	2.619 %		6.432	WEIGHT TAKEN	
TESTIS/EPIDID (TP)	4.85	.984 %		2.416	WEIGHT TAKEN	

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LIVER (LI) : -FOCI OF MONONUCLEAR CELLS,-MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)		
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD)		

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08406 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 515.8 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 10:27 PROSECTOR: TIM GROVE REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN		O R G A N S T A T U S
			WEIGHT	RATIO	
ADRENAL (AD)	.054	.0105 %	.0260		WEIGHT TAKEN
BRAIN W/STEM (BR)	2.07	.402 %	1.000		WEIGHT TAKEN
HEART (HT)	1.22	.237 %	.591		WEIGHT TAKEN
SPLEEN (SP)	.69	.133 %	.332		WEIGHT TAKEN
KIDNEY (KD)	3.08	.598 %	1.487		WEIGHT TAKEN
LIVER (LI)	12.85	2.490 %	6.194		WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.81	.933 %	2.319		WEIGHT TAKEN

P A T H O L O G Y O B S E R V A T I O N S
NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LI) :
-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID, SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LI), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RF), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ~COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 207

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08407 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 481.6 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 13:53 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	O R G A N S T A T U S	
				WEIGHT TAKEN	WEIGHT TAKEN
ADRENAL (AD)	.052	.0108 %	.0241	WEIGHT TAKEN	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.16	.449 %	1.000	WEIGHT TAKEN	WEIGHT TAKEN
HEART (HT)	1.30	.271 %	.603	WEIGHT TAKEN	WEIGHT TAKEN
SPLEEN (SP)	.77	.160 %	.357	WEIGHT TAKEN	WEIGHT TAKEN
KIDNEY (KO)	2.78	.578 %	1.288	WEIGHT TAKEN	WEIGHT TAKEN
LIVER (LI)	11.80	2.449 %	5.461	WEIGHT TAKEN	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.74	.984 %	2.194	WEIGHT TAKEN	WEIGHT TAKEN

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS: NONE

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID, -SLIGHT
-PNEUMONITIS, -MINIMAL

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SI), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (YW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08408 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 473.1 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 10:53 PROSECTOR: TIM GROVE REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	P A T H O L O G Y O B S E R V A T I O N S	HISTOPATHOLOGY
-APPEARED NORMAL	NECROPSY	
	^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SI), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08409 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 471.7 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 11:43 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHRITIS, CHRONIC PROGRESSIVE,-
MINIMAL
LUNG (LI) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 210

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08410 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 492.8 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 14:46 PROSECTOR: DOUGLAS HERMON
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP RECORDER: SID JONES, DVM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

EYE (EY) :

-GLOBE RUPTURED POST MORTEM; LEFT

^COLLECTED/TAKEN (XW) :

-ELECTRON MICROSCOPY SAMPLE; LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

EYE (EY) :

>UNREMARKABLE

KIDNEY (KD) :

-NEPHROPATHY, CHRONIC PROGRESSIVE, -

MINIMAL

LIVER (LI) :

-FOCI OF MONONUCLEAR CELLS, -MINIMAL

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,

INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO)
, LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLFN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LACRIMAL GL, EXO (EO)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	P A T H O L O G Y O B S E R V A T I O N S	HISTOPATHOLOGY
-RIGHT EYE-CHROMODACRYORRHEA; MALOCCLUSION	^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:RIGHT EYE- CHROMODACRYORRHEA, MALOCCLUSION	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BOVIE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)		
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)		

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 212

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08412 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 527.4 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 10:02 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHO, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHO, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XM) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LI) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UFSICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08413 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 506.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:20 PROSECTOR: TIM GROVE RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS	
				WEIGHT TAKEN	WEIGHT TAKEN
ADRENAL (AD)	.055	.0109 %	.0270	WEIGHT TAKEN	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.04	.403 %	1.000	WEIGHT TAKEN	WEIGHT TAKEN
HEART (HT)	1.30	.257 %	.637	WEIGHT TAKEN	WEIGHT TAKEN
SPLEEN (SP)	.72	.142 %	.353	WEIGHT TAKEN	WEIGHT TAKEN
KIDNEY (KD)	2.74	.542 %	1.343	WEIGHT TAKEN	WEIGHT TAKEN
LIVER (LI)	12.49	2.468 %	6.123	WEIGHT TAKEN	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.83	.955 %	2.368	WEIGHT TAKEN	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

APPEARED NORMAL

GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LU):
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-MINIMAL

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 214

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08414 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 528.3 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:19 PROSECTOR: TIM GROVE
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

HISTOPATHOLOGY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE: EXTERNAL OBSERVATIONS: NONE

KIDNEY (KO) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08415 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 460.6 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 12:19 PROSECTOR: DOUGLAS HERNDON RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	KIDNEY (KD) : -NEPHROPATHY, CHRONIC PROGRESSIVE, - MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (OS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 216

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08416 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: UNSCHEDULED (0)
DATE OF DEATH: 05/14/86 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: 425.6 GRAMS
DATE AND TIME OF NECROPSY: 05/14/86 11:57 PROSECTOR: TIM GRABUE RECORDER: JAMES CAMPBELL
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

BRAIN W/STEM (BR) :

-SOFT

LUNG (LU) :

-FAILURE TO COLLAPSE; ALL LOBES

GENERAL INFORMATION (XX) :

>NOTE:>LAST IN-LIFE AND EXTERNAL

OBSERVATIONS:NONE. FOUND DEAD

BEFORE DOSING

HISTOPATHOLOGY

BRAIN W/STEM (BR) :

>UNREMARKABLE

CECUM (CE) :

>TISSUE MISSING

COLON (CO) :

>TISSUE MISSING

DUODENUM (DU) :

>TISSUE MISSING

ILEUM (IL) :

>TISSUE MISSING

JEJUNUM (JE) :

>TISSUE MISSING

LUNG (LI) :

-PERIBRONCHIAL/PERIVASCULAR,

INFILTRATION, LYMPHOID,-SLIGHT

-FOREIGN MATERIAL,-PRESENT

RECTUM (RE) :

>TISSUE MISSING

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 217

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

STUDY NUMBER: 239911NR

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808416 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 05/14/86 STUDY DAY OF DEATH: 34 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: 425.6 GRAMS
DATE AND TIME OF NECROPSY: 05/14/86 11:57 PROSECTOR: TIM GROVE RECORDED: JAMES CANNON
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MONGEL (SU),
TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), *COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT),
KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MONGEL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 218

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: 808417 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: UNSCHEDULED (0)
DATE OF DEATH: 04/25/86 STUDY WEEK OF DEATH: 3 TERMINAL BODY WEIGHT: 305.5 GRAMS
DATE AND TIME OF NECROPSY: 04/25/86 14:35 PROSECTOR: JAMES CANNON RECORDER: JAMES CANNON
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

BRAIN W/STEM (BR) :
-SOFT; FOREBRAIN
LUNG (LU) :
-FAILURE TO COLLAPSE; ALL LOBES
GENERAL INFORMATION (XX) :
>NOTE:>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS: CONVULSIONS, FOUND
DEAD

HISTOPATHOLOGY

ADRENAL, MEDULLA (AM) :
-UNILATERALLY EXAMINED, -PRESENT
AORTA, THORACIC (AO) :
 >TISSUE MISSING
BRAIN W/STEM (BR) :
 >UNREMARKABLE
LUNG (LU) :
 -PERIBRONCHIAL/PERIVASCULAR,
 INFILTRATION, LYMPHOID, -SLIGHT
 -FOREIGN MATERIAL, -PRESENT
MAMMARY GLAND (MG) :
 >SECTION EXAMINED; TISSUE NOT PRESENT
NERVE, SCIATIC (SN) :
 >TISSUE MISSING
PROSTATE (PR) :
 -MONONUCLEAR CELL INFILTRATE, -SLIGHT

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08417 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: UNSCHEDULED (D)
 DATE OF DEATH: 04/25/86 STUDY DAY OF DEATH: 15 STUDY WEEK OF DEATH: 3 TERMINAL BODY WEIGHT: 305.5 GRAMS
 DATE AND TIME OF NECROPSY: 04/25/86 14:35 PROSECUTOR: JAMES CANNON RECORDER: JAMES CANNON
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB), RECTUM (DE),
 COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
 ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI),
 LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
 MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
 RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGEL (SI),
 TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ~COLLECTED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), BONE, FEMUR (FE), BONE, STERNUM (SB), CECUM (CE), COLON (CO), CORD, CERVICAL (CS),
 CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT),
 ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
 SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGEL (SI), TESTIS (TE), THYMUS (TH),
 THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808418 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 225.9 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:24 PROSECTOR: TIM GROVE REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.050	.0221 %	.0244	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.05	.907 %	1.000	WEIGHT TAKEN
HEART (HT)	1.27	.562 %	.620	WEIGHT TAKEN
SPLEEN (SP)	.74	.328 %	.361	WEIGHT TAKEN
KIDNEY (KD)	3.38	1.496 %	1.649	WEIGHT TAKEN
LIVER (LI)	13.30	5.888 %	6.488	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.90	2.169 %	2.398	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KD) :

-NEPHROPATHY, CHRONIC PROGRESSIVE, -MINIMAL

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTED: 12-MAY-86
PAGE: 221

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08419 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 499.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:03 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE: LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNGS (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)		
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)		

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTED: 12-MAY-88
PAGE: 222

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808420 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 443.2 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:10 PROSECTOR: DOUGLAS HERNDON
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP
WEIGHER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.048	.0109 %	.0221	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.19	.493 %	1.000	WEIGHT TAKEN
HEART (HT)	1.36	.308 %	.624	WEIGHT TAKEN
SPLEEN (SP)	.75	.170 %	.344	WEIGHT TAKEN
KIDNEY (KD)	2.71	.611 %	1.239	WEIGHT TAKEN
LIVER (LI)	10.94	2.468 %	5.005	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.91	1.334 %	2.705	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

-MALOCCLUSION

GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL

OBSERVATIONS: MALOCCLUSION

HISTOPATHOLOGY

KIDNEY (KD):
-NEPHROPATHY, CHRONIC PROGRESSIVE, -MINIMAL
-CORTICAL CYST, -PRESENT
LIVER (LI):
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
LUNG (LU):
-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -MINIMAL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08421 SEX: MALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 414.5 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:45 PROSECTOR: DOUGLAS HERNDON
POST-FTX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
SLIGHT
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUFED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 224

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808442 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 452.4 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:39 PROSECTOR: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUFD ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08443
SEX: MALE
DOSE GROUP: 3
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 481.1 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 10:50
PROSECTOR: DOUGLAS HERNDON
REORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: SID JONES, DVM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT PROSTATE (PR) : >UNREMARKABLE
PROSTATE (PR) : -DARK AREA; ONE, DARK RED, 1.0 X 0.5 CM >NOTE:>DARK AREA, POSSIBLE INJECTION SITE ^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 226

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08444 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 500.0 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 8:45 PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DUM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACVP WEIGHTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.042	.0884 %	.0181	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.32	.464 %	1.000	WEIGHT TAKEN
HEART (HT)	1.22	.244 %	.526	WEIGHT TAKEN
SPLEEN (SP)	.80	.160 %	.345	WEIGHT TAKEN
KIDNEY (KD)	3.37	.674 %	1.453	WEIGHT TAKEN
LIVER (LI)	13.50	2.700 %	5.819	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.38	1.076 %	2.319	WEIGHT TAKEN

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS
NECROPSY

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KD) :

-NEPHROPATHY, CHRONIC PROGRESSIVE,-

SLIGHT

LUNG (LL) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC. APPENDIX 8 PRINTED: 12-MAY-88
 DEPARTMENT OF PATHOLOGY *** PATH/TOX SYSTEM OUTPUT *** PAGE: 227
 SUBCHRONIC TOXICITY STUDY IN RATS STUDY NUMBER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08445 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 455.1 GRAMS
 DATE AND TIME OF NECROPSY: 07/14/86 12:00 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		
CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
 LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
 MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
 PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
 SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
 URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808446 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D) STUDY NUMBER: 2399108
DATE OF DEATH: 04/30/86 STUDY WEEK OF DEATH: 3 TERMINAL BODY WEIGHT: 316.7 GRAMS
DATE AND TIME OF NECROPSY: 04/30/86 15:50 PROSECTOR: BARBARA DAY RECORDER: BARBARA DAY
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	P A T H O L O G Y O B S E R V A T I O N S	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU) : -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES, LIGHT TO DARK RED GENERAL INFORMATION (XX) : >NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS:NONE. DIED SHORTLY AFTER DOSING	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL PARATHYROID (PT) : >TISSUE MISSING PROSTATE (PR) : -MONONUCLEAR CELL INFILTRATE,-SLIGHT THYROID (TY) : >TISSUE MISSING

STUDY NUMBER: 2199108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808446 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D) TERMINAL BODY WEIGHT: 316.7 GRAMS
DATE OF DEATH: 04/30/86 STUDY DAY OF DEATH: 3 PROSECTOR: BARBARA DAY RECORDER: BARBARA DAY
DATE AND TIME OF NECROPSY: 04/30/86 15:58 PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHER: NOT REQUIRED BY PROTOCOL
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SO), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), *COLLECTED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), RECTUM (RE),
SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 230

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08447 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 468.5 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:49 PROSECTOR: DOUGLAS HERNDON
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

CLINICAL OBSERVATIONS

-MALOCCLUSION

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE: >EXTERNAL
OBSERVATIONS: MALOCCLUSION

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
-PYELONEPHRITIS, -SLIGHT
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (OS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUFED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08448 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 05/14/86 STUDY DAY OF DEATH: 34 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: 362.4 GRAMS
DATE AND TIME OF NECROPSY: 05/14/86 12:05 PROSECTOR: BARBARA DAY
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	P A T H O L O G Y O B S E R V A T I O N S	HISTOPATHOLOGY
-APPEARED NORMAL	NECROPSY BRAIN W/STEM (BR) : -SOFT LUNG (LU) : -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES, LIGHT TO DARK RED GENERAL INFORMATION (XX) : >NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS:NONE. FOUND DEAD BEFORE DOSING	BRAIN W/STEM (BR) : >UNREMARKABLE CECUM (CE) : >AUTOLYTIC COLON (CO) : >AUTOLYTIC DUODENUM (DI) : >AUTOLYTIC ILEUM (IL) : >AUTOLYTIC JEJUNUM (JE) : >AUTOLYTIC LUNG (LU) : -FOREIGN MATERIAL,-PRESENT MAMMARY GLAND (MG) : >SECTION EXAMINED; TISSUE NOT PRESENT RECTUM (RE) : >AUTOLYTIC

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 232

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08448 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 05/14/86 STUDY DAY OF DEATH: 34 STUDY WEEK OF DEATH: 5 TERMINAL BODY WEIGHT: 362.4 GRAMS
DATE AND TIME OF NECROPSY: 05/14/86 12:05 PROSECTOR: BARBARA DAY RECORDER: JAMES CAMPION
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), Cecum (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (FO), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOMEL (SH),
TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT),
KIDNEY (KD), LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOMEL (SH), TESTIS (TF), THYMUS (TH),
THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2392108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08449 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 423.1 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 11:35 PROSECTOR: TIM GROVE RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS	
				WEIGHT TAKEN	WEIGHT TAKEN
ADRENAL (AD)	.044	.0195 %	.0227	WEIGHT TAKEN	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.95	.461 %	1.000	WEIGHT TAKEN	WEIGHT TAKEN
HEART (HT)	1.17	.278 %	.602	WEIGHT TAKEN	WEIGHT TAKEN
SPLEEN (SP)	.75	.177 %	.383	WEIGHT TAKEN	WEIGHT TAKEN
KIDNEY (KO)	2.79	.668 %	1.429	WEIGHT TAKEN	WEIGHT TAKEN
LIVER (LI)	10.21	2.412 %	5.227	WEIGHT TAKEN	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.94	1.167 %	2.530	WEIGHT TAKEN	WEIGHT TAKEN

CLINICAL OBSERVATIONS
NECROPSY
HISTOPATHOLOGY

GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERVATIONS:NONE
LUNG (LU):
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELTAL (SM), NERVE, SCIATIC (SH), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KO), LIVER (LI)

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-83
PAGE: 234

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808450 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 05/31/86 STUDY WEEK OF DEATH: 8 TERMINAL BODY WEIGHT: 450.8 GRAMS
DATE AND TIME OF NECROPSY: 05/31/86 14:05 PROSECTOR: BARBARA DAY REORDER: BARBARA DAY
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

LUNG (LU) :

-FAILURE TO COLLAPSE; ALL LOBES
-MOTTLED; ALL LOBES, LIGHT TO DARK RED

GENERAL INFORMATION (XX) :

>NOTE:>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS:NONE. FOUND DEAD AT
ONE HOUR POST-DOSE OBSERVATIONS.

ILEUM (IL) :

>AUTOLYTIC

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT
-FOREIGN MATERIAL,-PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), *COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08451
SEX: MALE
DOSE GROUP: 3
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86
STUDY DAY OF DEATH: 96
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 449.0 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 10:26
PROSECTOR: BARBARA DAY
REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: SID JONES, DUM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHRUPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 236

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08452 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 433.6 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:20 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

KIDNEY (KO) :
-PELVIS, DILATED; BOTH, MODERATELY
^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KO) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
SLIGHT
-PELVIS, DILATATION, -MODERATE
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAID SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, RL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08453
SEX: MALE
DOSE GROUP: 3
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86
STUDY DAY OF DEATH: 97
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 439.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:50
PROSECTOR: BARBARA DAY
RECORDED: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: SID JONES, DVM, PHD, DACVP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	KIDNEY (KD) : -NEPHROPATHY, CHRONIC PROGRESSIVE, - MINIMAL LUNG (LI) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT -FOREIGN MATERIAL, -PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 238

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08454 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 04/29/86 STUDY DAY OF DEATH: 19 STUDY WEEK OF DEATH: 3 TERMINAL BODY WEIGHT: 333.8 GRAMS
DATE AND TIME OF NECROPSY: 04/29/86 16:17 PROSECTOR: BARBARA DAY RECORDER: BARBARA DAY
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

LUNG (LU) :
-FAILURE TO COLLAPSE; ALL LOBES
-MOTTLED; ALL LOBES, LIGHT TO DARK RED
TESTIS (TE) :
-UNEQUALLY SIZED; LEFT, SMALL
GENERAL INFORMATION (XX) :
>NOTE:>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS:NONE. FOUND DEAD
ONE HOUR AFTER DOSING

HISTOPATHOLOGY

LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, SLIGHT
-FOREIGN MATERIAL, -PRESENT
TESTIS (TE) :
>UNREMARKABLE

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08454 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 04/29/86 STUDY DAY OF DEATH: 19 STUDY WEEK OF DEATH: 3 TERMINAL BODY WEIGHT: 333.8 GRAMS
DATE AND TIME OF NECROPSY: 04/29/86 16:17 PROSECTOR: BARBARA DAY RECORDER: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHT: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), *COLLECTED/TAKEN (X&J)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808455 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 463.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:33 PROSECUTOR: BARBARA DAY RECORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACVP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-BOTH EYES-CHROMODACRYORRHEA

^COLLECTED/TAKEN (XU) :

-ELECTRON MICROSCOPY SAMPLE; LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS: BOTH EYES-
CHROMODACRYORRHEA

HISTOPATHOLOGY

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TF), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808456 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 495.9 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:28 PROSECTOR: DOUGLAS HERNDON RECIPIENT: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

HISTOPATHOLOGY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :

-ELECTRON MICROSCOPY SAMPLE; LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SPINAL VERTEBRAL (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399100

ANIMAL NUMBER: B08457 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 530.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:09 PROSECTOR: BARBARA DAY RECIPIER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.060	.0113 %	.0289	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.07	.389 %	1.000	WEIGHT TAKEN
HEART (HT)	1.17	.220 %	.565	WEIGHT TAKEN
SPLEEN (SP)	.63	.119 %	.306	WEIGHT TAKEN
KIDNEY (KO)	3.48	.656 %	1.685	WEIGHT TAKEN
LIVER (LI)	12.24	2.306 %	5.925	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.04	.948 %	2.437	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KO) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -SLIGHT
-GLomerular casts, -SLIGHT
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

APPENDIX 8
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 243

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

STUDY NUMBER: 239910H

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808457 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 TERMINAL BODY WEIGHT: 530.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:09 PROSECTOR: BARBARA DAY RETAINER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 244

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08458 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 04/14/86 STUDY DAY OF DEATH: 4 STUDY WEEK OF DEATH: 1 TERMINAL BODY WEIGHT: 216.1 GRAMS
DATE AND TIME OF NECROPSY: 04/14/86 12:30 PROSECTOR: KIM LINCOLN RECORDER: KIM LINCOLN
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

LUNG (LJ) :

-FAILURE TO COLLAPSE; ALL LOBES
-MOTTLED; ALL LOBES, WHITE TO RED
GENERAL INFORMATION (XX) :
>NOTE:>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS:NONE

HISTOPATHOLOGY

ADRENAL, CORTEX (AC) :
-UNILATERALLY EXAMINED,-PRESENT
ADRENAL, MEDULLA (AM) :
-UNILATERALLY EXAMINED,-PRESENT
CECUM (CE) :
>AUTOLYTIC
COLON (CO) :
>AUTOLYTIC
DUODENUM (DU) :
>AUTOLYTIC
EYE (EY) :
>AUTOLYTIC
ILEUM (IL) :
>AUTOLYTIC
JEJUNUM (JE) :
>AUTOLYTIC
LUNG (LJ) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT
-CONGESTION,-MODERATE
-FOREIGN MATERIAL,-PRESENT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT
RECTUM (RE) :
>AUTOLYTIC
STOMACH, GL (ST) :
>AUTOLYTIC
URINARY BLADDER (UB) :
>AUTOLYTIC

APPENDIX 8
 *** PATH/TOX SYSTEM OUTPUT ***
 SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
 PAGE: 245

HAZLETON LABORATORIES AMERICA, INC.
 DEPARTMENT OF PATHOLOGY

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08458 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D) TERMINAL BODY WEIGHT: 216.1 GRAMS
 DATE OF DEATH: 04/14/86 STUDY DAY OF DEATH: 4 STUDY WEEK OF DEATH: 1 REORDER: KIM LINCOLN
 DATE AND TIME OF NECROPSY: 04/14/86 12:30 PROSECTOR: KIM LINCOLN WEIGHER: NOT REQUIRED BY PROTOCOL
 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
 LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
 PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
 STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CORD, CERVICAL (CS),
 CORD, LUMBAR (LC), CORD, THORACIC (TC), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), KIDNEY (KD), LACRIMAL GL, EXO (EO)
 , LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
 MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), SEMINAL VESICLE (SV),
 SKIN (SK), SPLEEN (SP), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08459 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 495.7 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:57 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LU) :
-PULMONARY PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2199108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08460 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 495.7 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 8:19 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.063	.0127 %	.0297	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.12	.428 %	1.000	WEIGHT TAKEN
HEART (HT)	1.30	.262 %	.612	WEIGHT TAKEN
SPLEEN (SP)	.94	.189 %	.443	WEIGHT TAKEN
KIDNEY (KD)	3.17	.640 %	1.497	WEIGHT TAKEN
LIVER (LI)	13.43	2.710 %	6.338	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.39	1.086 %	2.541	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	KIDNEY (KD) : -NEPHROPATHY, CHRONIC PROGRESSIVE,- MINIMAL LIVER (LI) : -FOCI OF MONONUCLEAR CELLS,-MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
 LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
 MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
 PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
 SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONAL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
 URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

SUBCHRONIC TOXICITY STUDY IN RATS

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08461 SEX: MALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 503.6 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 11:49 PROSECTOR: TIM GROVE RECIPIENT: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.072	.0143 %	.0365	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.97	.391 %	1.000	WEIGHT TAKEN
HEART (HT)	1.39	.276 %	.706	WEIGHT TAKEN
SPLEEN (SP)	.81	.161 %	.411	WEIGHT TAKEN
KIDNEY (KD)	3.54	.703 %	1.797	WEIGHT TAKEN
LIVER (LI)	14.56	2.891 %	7.391	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.02	.997 %	2.548	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX):

>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KO):

-PYELONEPHRITIS,-SLIGHT

LUNG (LU):

-PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID,-MINIMAL

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD),
 LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
 MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
 PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
 SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
 URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08482 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 TERMINAL BODY WEIGHT: 466.3 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 8:56 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.047	.0101 %	.0219	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.15	.461 %	1.000	WEIGHT TAKEN
HEART (HT)	1.24	.266 %	.577	WEIGHT TAKEN
SPLEEN (SP)	.76	.163 %	.353	WEIGHT TAKEN
KIDNEY (KD)	3.52	.755 %	1.637	WEIGHT TAKEN
LIVER (LI)	13.30	2.852 %	6.186	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.95	1.062 %	2.382	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU) : -DARK AREA; LEFT APICAL LOBE, POSTERIOR AREA, DARK RED, 1.0 X 1.0 CM GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	BONE, FEMUR (FE) : -ARTICULAR SURFACE NOT PRESENT, -PRESENT LIVER (LI) : -(MULTI)FOCAL NECROSIS, -MODERATE LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

INDIVIDUAL ANIMAL SUMMARY REPORT
STUDY NUMBER: 2399108

ANIMAL NUMBER: B08482
SEX: MALE
DOSE GROUP: 4
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86
STUDY DAY OF DEATH: 95
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 466.3 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 8:56
PROSECTOR: BARBARA DAY
RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: SID JONES, DUM, PHD, DACUP
WEIGHER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYROID (TH), TRACHEA (TR), URINARY BLADDER (UB), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV),
SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08483 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 452.5 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:40 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-RIGHT EYE-CHROMODACRYORRHEA

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:RIGHT EYE-
CHROMODACRYORRHEA

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LIVER (LT) :
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
HIFILTRATION, LYMPHOID, -SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 252

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08483 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 452.5 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:40 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08484 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 451.8 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 11:12 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	BONE, FEMUR (FE) : -ARTICULAR SURFACE NOT PRESENT, -PRESENT KIDNEY (KD) : -NEPHROPATHY, CHRONIC PROGRESSIVE, - MINIMAL LIVER (LI) : -(MULTI)FOCAL NECROSIS, -SLIGHT LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08484 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 651.8 GRAMS
 DATE AND TIME OF NECROPSY: 07/14/86 11:12 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
 LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
 MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
 PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RF), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
 SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
 URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
 COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP),
 ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS),
 MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN),
 PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RF), SEMINAL VESICLE (SV), SKIN (SK),
 SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
 URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 255

STUDY NUMBER: 2199108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808485 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 359.5 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:07 PROSECTOR: TIM GROVE REFORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.053	.0147 %	.0277	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.91	.531 %	1.000	WEIGHT TAKEN
HEART (HT)	1.09	.304 %	.571	WEIGHT TAKEN
SPLEEN (SP)	.63	.174 %	.327	WEIGHT TAKEN
KIDNEY (KD)	3.01	.838 %	1.578	WEIGHT TAKEN
LIVER (LI)	10.82	3.009 %	5.663	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.53	1.260 %	2.370	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
SLIGHT
LUNG (LI) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
MAMMARY GLAND (MG) :
>SECTION EXAMINED: TISSUE NOT PRESENT

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 256

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08485 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 359.5 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:07 PROSECTOR: TIM GROVE REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), *COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV),
SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08486

SEX: MALE

DOSE GROUP: 4

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 95

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 444.2 GRAMS

DATE AND TIME OF NECROPSY: 07/14/86 13:33

PROSECTOR: TIM GROVE

REORDER: SID JONES, DUM, PHD, DACUP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.053	.0119 %	.0263	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.00	.451 %	1.000	WEIGHT TAKEN
HEART (HT)	1.13	.254 %	.563	WEIGHT TAKEN
SPLEEN (SP)	.54	.120 %	.267	WEIGHT TAKEN
KIDNEY (KD)	3.15	.710 %	1.574	WEIGHT TAKEN
LIVER (LI)	13.27	2.987 %	6.623	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.57	1.253 %	2.779	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
<div> <div>APPEARED NORMAL</div> <div>GENERAL INFORMATION (XX) :</div> <div>>NOTE:>EXTERNAL OBSERVATIONS:NONE</div> </div>	<div> <div>NECROPSY</div> <div>EYE (EY) :</div> <div>-CHRONIC INFLAMMATION, HARDERIAN GLAND,-</div> <div>SLIGHT</div> <div>LUNG (LU) :</div> <div>-PERIBRONCHIAL/PERIVASCULAR,</div> <div>INFILTRATION, LYMPHOID,-SLIGHT</div> </div>	

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 258

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08486 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 444.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:33 PROSECTOR: TIM GROVE RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXD (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-83
PAGE: 259

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08487 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 431.0 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:52 PROSECUTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-RIGHT EYE-CHROMODACRYORRHEA; NOSE-BLOODY CRUST

NECROPSY

KIDNEY (KO) :
-PELVIS, DILATED; LEFT, SLIGHTLY
^COLLECTED/TAKEN (XU) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:RIGHT EYE-
CHROMODACRYORRHEA, NOSE-BLOODY
CRUST

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE,-
MINIMAL
-GRANULAR CASTS,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SA),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SA),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 260

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2799108

ANIMAL NUMBER: B08488 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 374.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 9:07 PROSECTOR: TIM GROVE RECORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

KIDNEY (KD) :
-PELVIS, DILATED; BOTH, MODERATELY
-PELVIS, FLUID; RIGHT, MILKY
-PELVIS, GRANULAR MATERIAL; BOTH,
WHITE, PINPOINT
^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-PELVIS, DILATATION, -MODERATELY SEVERE
-PYELONEPHRITIS, -MODERATELY SEVERE
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
MARROW, STERNUM (SE) :
-HYPERCELLULAR, -MODERATE
PROSTATE (PR) :
-INFLAMMATION, CHRONIC ACTIVE, -MODERATE
SEMINAL VESICLE (SV) :
-INFLAMMATION, CHRONIC ACTIVE, -MODERATE
URINARY BLADDER (UB) :
-CALCULUS, -PRESENT
-MICROCAL HYPERPLASIA, -SEVERE

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08488 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 374.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 9:07 PROSECTOR: TIM GROVE
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 262

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08489 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 373.1 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 10:34 PROSECTOR: DOUGLAS HFRINDIN RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LID) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOCYTES, SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SI), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SI), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808490

SEX: MALE

DOSE GROUP: 4

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 95

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 405.0 GRAMS

DATE AND TIME OF NECROPSY: 07/14/86 14:54

PROSECTOR: BARBARA DAY

RECORDER: SID JONES, DUM, PHD, DACUP

POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.046	.0114 %	.0232	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.99	.492 %	1.000	WEIGHT TAKEN
HEART (HT)	1.03	.254 %	.517	WEIGHT TAKEN
SPLEEN (SP)	.70	.173 %	.352	WEIGHT TAKEN
KIDNEY (KD)	2.96	.732 %	1.487	WEIGHT TAKEN
LIVER (LI)	10.49	2.591 %	5.264	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.51	1.114 %	2.263	WEIGHT TAKEN

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS

NECROPSY

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LIVER (LI) :

- (MULTI)FOCAL NECROSIS, -MODERATE

LUNGS (LU) :

-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -MINIMAL

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 264

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08490 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 405.0 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 14:54 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PRISTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08491 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: UNSCHEDULED (D) TERMINAL BODY WEIGHT: 287.1 GRAMS
DATE OF DEATH: 06/05/86 STUDY WEEK OF DEATH: 8
DATE AND TIME OF NECROPSY: 06/05/86 7:45 PROSECUTOR: BARBARA DAY RECORDER: BARBARA DAY
POST-FTX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	LUNG (LU) : -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES, LIGHT TO DARK RED STOMACH, GL (ST) : -PALE AREA; FUNDIC MUCOSA, SEVERAL, LINEAR, WHITE, 4 X 2 MM TO 1.0 X 0.2 CM GENERAL INFORMATION (XX) : >NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -FOREIGN BODY PNEUMONIA,-MODERATE PANCREAS (PA) : -INFLAMMATION, CHRONIC,-MINIMAL STOMACH, GL (ST) : >UNREMARKABLE

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 266

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399103

ANIMAL NUMBER: B08491 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 06/05/86 STUDY DAY OF DEATH: 56 STUDY WEEK OF DEATH: 8 TERMINAL BODY WEIGHT: 287.1 GRAMS
DATE AND TIME OF NECROPSY: 06/05/86 7:45 PROSECTOR: BARBARA DAY RECTOR: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHT: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, NONGL (SU),
TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH),
THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2199100

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08492; SEX: MALE; DOSE GROUP: 4; SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86; STUDY WEEK OF DEATH: 14; TERMINAL BODY WEIGHT: 435.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:35; PROSECTOR: DOUGLAS HERNDON; REORDER: STD JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL; PATHOLOGIST: STD JONES, DUM, PHD, DACUP; WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KO) :
-NEPHROPATHY, CHRONIC PROGRESSIVE,
MINIMAL
LUNG (LI) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE),
SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH),
THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 263

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808493 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 04/27/86 STUDY DAY OF DEATH: 17 STUDY WEEK OF DEATH: 3 TERMINAL BODY WEIGHT: 317.0 GRAMS
DATE AND TIME OF NECROPSY: 04/27/86 13:47 PROSECTOR: TIM GROVE REORDER: TIM GROVE
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

HISTOPATHOLOGY

LUNG (LU) :

-FAILURE TO COLLAPSE; ALL LOBES

-MOTTLED; ALL LOBES, TAN TO DARK RED

GENERAL INFORMATION (XX) :

>NOTE:>LAST IN-LIFE AND EXTERNAL

OBSERVATIONS:CONVULSIONS, FOUND

DEAD

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR

INFILTRATION, LYMPHOID,-SLIGHT

-CONGESTION,-MODERATE

-FOREIGN MATERIAL,-PRESENT

MAMMARY GLAND (MG) :

>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SO), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08494 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 415.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:10 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACVP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT
NECROPSY	
^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:	
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)	
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:	
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)	

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-81
PAGE: 270

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399188

ANIMAL NUMBER: 808495 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 14 TERMINAL BODY WEIGHT: 406.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:13 PROSECTOR: BARBARA DAY REFORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

HISTOPATHOLOGY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KO) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LD) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08495 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 406.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:13 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), NERVE, SCIATIC (SN), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIUM, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTED: 12-MAY-88
PAGE: 272

STUDY NUMBER: 2199100

ANIMAL NUMBER: 808496 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 444.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:28 PROSECUTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.041	.0091 %	.0215	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.88	.423 %	1.000	WEIGHT TAKEN
HEART (HT)	1.05	.235 %	.556	WEIGHT TAKEN
SPLEEN (SP)	.63	.141 %	.334	WEIGHT TAKEN
KIDNEY (KD)	3.13	.703 %	1.662	WEIGHT TAKEN
LIVER (LI)	13.02	2.926 %	6.924	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.39	.987 %	2.345	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LIVER (LI) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, -LYMPHOID, -SIGHT
MAMMARY GLAND (MG) :
>SECTION EXAMINED; TISSUE NOT PRESENT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808496 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 444.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:28 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGL (SU), TESTIS (TE), THYROID (TH), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXD (EO),
LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGL (SU), TESTIS (TE), THYROID (TH), TRACHEA (TR),
URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
 SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
 PAGE: 274

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08497 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHMIDT, TERMINAL SACRIFICE
 DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 449.7 GRAMS
 DATE AND TIME OF NECROPSY: 07/15/86 11:37 PROSECTOR: BARBARA DAY REFERRED: SID JONES, DVM, PhD, DATUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DATUP WEIGHT: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.056	.0125 %	.0298	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.89	.421 %	1.000	WEIGHT TAKEN
HEART (HT)	1.00	.223 %	.530	WEIGHT TAKEN
SPLEEN (SP)	.59	.131 %	.311	WEIGHT TAKEN
KIDNEY (KD)	3.27	.727 %	1.728	WEIGHT TAKEN
LIVER (LI)	11.32	2.518 %	5.984	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.98	1.107 %	2.630	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LID) :

-PERIBRONCHIAL/PERIVASCULAR,
 INFILTRATION, LYMPHOID,-SLIGHT

PROSTATE (PR) :

-MONONUCLEAR CELL INFILTRATE,-SLIGHT

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08497 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 449.7 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:37 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08498 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 451.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:22 PROSECTOR: RAREARA DAY RETURNER: SID JONES, DVM, PhD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y R E S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
MAMMARY GLAND (MS) :
>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SI), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SO),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SI), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08499 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 433.5 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 12:11 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LJ) :
-PERITONIC/PERICARDIAL AR,
INFILTRATION, LYMPHOID,-SLIGHT
MAMMARY GLAND (MS) :
>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SC), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONAL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SC), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONAL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED FOR THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 278

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 9394188

ANIMAL NUMBER: 808500 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 443.4 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:20 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.052	.0117 %	.0243	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.14	.483 %	1.000	WEIGHT TAKEN
HEART (HT)	1.10	.248 %	.514	WEIGHT TAKEN
SPLEEN (SP)	.91	.205 %	.425	WEIGHT TAKEN
KIDNEY (KD)	3.24	.731 %	1.514	WEIGHT TAKEN
LIVER (LI)	14.54	3.279 %	6.794	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.40	1.218 %	2.523	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

LIVER (LI):
-RAISED AREA; LEFT LATERAL LOBE, ONE, TAN, DARK RED, 8 X 5 MM
>NOTE:>DARK AREA, POSSIBLE INJECTION SITE

HISTOPATHOLOGY

LIVER (LI):
-INJECTION SITE; -PRESENT
LUNGS (LD):
-PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID, -MINIMAL
PARATHYROID (PT):
>SECTION EXAMINED; TISSUE NOT PRESENT

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808500 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 443.4 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 8:20 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SR),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), COLLECTED, TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SR), MARROW, STERNUM (SF),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE),
SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH),
THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08501 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 428.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 13:47 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACVP WEIGHTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	O R G A N	
				S T A T U S	
ADRENAL (AD)	.063	.0146 %	.0300	WEIGHT TAKEN	
BRAIN W/STEM (BR)	2.09	.489 %	1.000	WEIGHT TAKEN	
HEART (HT)	1.34	.312 %	.639	WEIGHT TAKEN	
SPLEEN (SP)	.65	.152 %	.310	WEIGHT TAKEN	
KIDNEY (KD)	3.41	.796 %	1.630	WEIGHT TAKEN	
LIVER (LI)	13.29	3.105 %	6.356	WEIGHT TAKEN	
TESTIS/EPIDID (TP)	5.86	1.369 %	2.801	WEIGHT TAKEN	

CLINICAL OBSERVATIONS

-APPEARED NORMAL

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

MAMMARY GLAND (MB) :

>SECTION EXAMINED; TISSUE NOT PRESENT
PARATHYROID (PT) :

>SECTION EXAMINED; TISSUE NOT PRESENT
URINARY BLADDER (UB) :

>TISSUE MISSING

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 281

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08501 SEX: MALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 428.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 13:47 PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (XN), TESTIS (TE), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XN)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE),
SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), STOMACH, GL (ST), STOMACH, NONGL (XN), TESTIS (TE), THYROID (TY), TRACHEA (TR)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PFR THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 282

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2199108

ANIMAL NUMBER: B08382 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 278.5 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:21 PROSECTOR: BARBARA DAY REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.050	.0180 %	.0248	WEIGHT TAKEN
OVARY (OV)	.110	.0395 %	.0545	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.02	.725 %	1.0000	WEIGHT TAKEN
HEART (HT)	.68	.244 %	.337	WEIGHT TAKEN
SPLEEN (SP)	.52	.187 %	.257	WEIGHT TAKEN
KIDNEY (KD)	1.66	.596 %	.822	WEIGHT TAKEN
LIVER (LI)	6.67	2.395 %	3.302	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LL) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
INFILTRATION (IT) :
-DILATATION, -SLIGHT

STUDY NUMBER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08382 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 TERMINAL BODY WEIGHT: 278.5 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:21 PROSECTOR: BARBARA DAY REFERRED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ACCUMULATED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 284

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2499108

ANIMAL NUMBER: B08383 SEX: FEMALE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95
DATE AND TIME OF NECROPSY: 07/14/86 10:21
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL

DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
STUDY WEEK OF DEATH: 14
PROSECTOR: TIM GROVE
PATHOLOGIST: SID JONES, DVM, PhD, DACVP
WEIGHTER: NOT REQUIRED BY PROTOCOL

TERMINAL BODY WEIGHT: 247.1 GRAMS
RECORDED: SID JONES, DVM, PhD, DACVP

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

HISTOPATHOLOGY

EYE (EY) :

-GLOBE RIPTURED POST MORTEM; RIGHT
-COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE: EXTERNAL OBSERVATIONS: NONE

EYE (EY) :

>UNREMARKABLE
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, SLIGHT
PNEUMOTHORAX (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT
PITUITARY (PT) :
>TISSUE MISSING

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERUTAL (CS), CORO, LUMBAR (LO), CORO, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRON, STERNUM (SF),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, BL (ST), STOMACH, MENS (SD), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERUTAL (CS), CORO, LUMBAR (LO), CORO, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRON, STERNUM (SF), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, BL (ST),
STOMACH, NONEL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808384

SEX: FEMALE

DOSE GROUP: 1

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 14

TERMINAL BODY WEIGHT: 297.1 GRAMS

DATE AND TIME OF NECROPSY: 07/14/86 12:57

PROSECTOR: BARBARA DAY

RECORDER: SID JONES, DVM, PhD, DACUP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DVM, PhD, DACUP

WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.084	.0281 %	.0414	WEIGHT TAKEN
OVARY (OU)	.058	.0196 %	.0289	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.02	.679 %	1.000	WEIGHT TAKEN
HEART (HT)	.85	.288 %	.423	WEIGHT TAKEN
SPLEEN (SP)	.58	.196 %	.288	WEIGHT TAKEN
KIDNEY (KD)	1.79	.604 %	.839	WEIGHT TAKEN
LIVER (LI)	6.58	2.216 %	3.263	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

CLINICAL OBSERVATIONS

-RIGHT EYE-CHROMODACRYORRHEA; MALOCCLUSION

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL

OBSERVATIONS: MALOCCLUSION, RIGHT EYE-CHROMODACRYORRHEA

LUNGS (LU) :

-PERIPHERAL/PERIVASCULAR INFILTRATION, LYMPHOID, -SLIGHT QUARY (QU) :

-UNILATERALLY EXAMINED, -PRESENT PITUITARY (PT) :

-CYST, -PRESENT

HISTOPATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 284

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 23991HB

ANIMAL NUMBER: B08384 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 297.1 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 12:57 PRISECTOR: BARBARA DAY RECIPIER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, FXD (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNCOLLECTED-TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, FXD (FD),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 287

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808185 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 262.4 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:40 PROSECTOR: DOUGLAS HERNDON RETORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS	WEIGHT TAKEN
ADRENAL (AD)	.058	.0220 %	.0292		WEIGHT TAKEN
OVARY (OV)	.151	.0576 %	.0766		WEIGHT TAKEN
BRAIN W/STEM (BR)	1.97	.752 %	1.000		WEIGHT TAKEN
HEART (HT)	1.05	.399 %	.530		WEIGHT TAKEN
SPLEEN (SP)	.41	.157 %	.209		WEIGHT TAKEN
KIDNEY (KD)	2.00	.761 %	1.012		WEIGHT TAKEN
LIVER (LT)	7.07	2.696 %	3.585		WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

UTERUS (UT) :
-LUMEN, FLUID; BOTH HORNS, CLEAR
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS: NONE

HISTOPATHOLOGY

LUNGS (LID) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
UTERUS (UT) :
-DILATATION, -MODERATE

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 288

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 279918A

ANIMAL NUMBER: B08385 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 262.4 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:40 PROSECTOR: DOUGLAS HERNDON REFERRED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MURAL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

INDIVIDUAL ANIMAL SUMMARY REPORT

BU 1663 : 33 JUL 19 1965

ANIMAL NUMBER: B08186
DATE OF DEATH: 07/15/86
DATE AND TIME OF NECROPSY: 07/15/86 9:19
SEX: FEMALE
STUDY DAY OF
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL

DOSE GROUP: 1 SACRIFICE STATUS: SACRIFICED, TERMINAL SACRIFICE
: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 243.6 GRAMS
PROSECTOR: DONALD ASHERDAIN REFORMER: SID JAMES, DUM, PHD, DACUP
PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS:
NECROPSY

CLINICAL OBSERVATIONS

-----APPEARED NORMAL

KIDNEY (KD) : BOTH, SEUFRAL, TAN, 1 X 1
-PALE AREA; MM

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KO) :
 > UNREMARKABLE
 LIVER (LI) :
 - FATTY OF MODERATE DEGREE
 LUNG (LU) :
 - PERIBRONCHIAL-PERIVASCULAR,
 INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

[illegible]

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

FOLLOWING TISSUES WERE OBTAINABLE BY AUTOPSY: ADRENAL (AD), AORTA, THORACIC (AO), AIRIE, FEMUR (FE), RIBIE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EG),
 LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SM),
 NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PLEURAL (PL), RECTUM (RE), SKIN (SK),
 SPLEEN (SP), STOMACH, GL (ST), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
 UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAID ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2499188

ANIMAL NUMBER: B08387 SEX: FEMALE NOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 252.0 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 15:07 PROSECTOR: TIM GROVE REFORMER: SID JONES, DUM, PHD, DATUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DATUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.062	.0240 %	.0310	WEIGHT TAKEN
OVARY (OV)	.124	.0482 %	.0623	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.99	.774 %	1.0000	WEIGHT TAKEN
HEART (HT)	.84	.326 %	.422	WEIGHT TAKEN
SPLEEN (SP)	.56	.218 %	.281	WEIGHT TAKEN
KIDNEY (KD)	1.73	.673 %	.820	WEIGHT TAKEN
LIVER (LI)	6.24	2.430 %	3.341	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

ADRENAL, CORTEX (AC) :
-DEGENERATION, MINIMAL
EYE (EY) :
-CHRONIC INFLAMMATION, HARDERIAN GLAND, SLIGHT
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, MINIMAL
LUNG (LU) :
-PERIBRONCHIAL PERIVASCULAR INFILTRATION, LYMPHOID, SLIGHT

STUDY NUMBER: 2492188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08387 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 257.0 GRAMS
 DATE AND TIME OF NECROPSY: 07/14/86 15:07 PROSECTOR: TIM GROVE RECORDER: SID JONES, DUM, PHD, DADUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DADUP MEASURER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SE),
 BRAIN W/STEM (BR), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TE),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
 LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
 PITUITARY (PI), RECTUM (RE), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SU),
 THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT), COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SE), BRAIN W/STEM (BR), CECUM (CE),
 COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TE), DUODENUM (DU), ESOPHAGUS (ES), HEART (HT),
 ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), MAMMARY GLAND (MG),
 MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA),
 PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SU),
 THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 292

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 7399108

ANIMAL NUMBER: 808388 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 251.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 15:13 PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.048	.0192 %	.0256	WEIGHT TAKEN
OVARY (OV)	.090	.0359 %	.0479	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.88	.750 %	1.000	WEIGHT TAKEN
HEART (HT)	.89	.354 %	.471	WEIGHT TAKEN
SPLEEN (SP)	.64	.256 %	.342	WEIGHT TAKEN
KIDNEY (KO)	1.68	.667 %	.839	WEIGHT TAKEN
LIVER (LT)	6.62	2.634 %	3.511	WEIGHT TAKEN

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS

GENERAL INFORMATION (XX):
>NOTE: EXTERNAL OBSERVATIONS: NONE

HISTOPATHOLOGY

LUNG (LU):
-PULMONARY PERIVASCULAR,
INFILTRATION, LYMPHOID, -SIGHT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 293

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2492108

ANIMAL NUMBER: B08388 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 251.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 15:13 PROSECTOR: DOUGLAS HERNDON PATHOLOGIST: SID JONES, DUM, PHD, DACUP RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXN (EL),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (NU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT), UNIDENTIFIED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXN (EL),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (NU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 294

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399100

ANIMAL NUMBER: 808389 SEX: FEMALE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96
DATE AND TIME OF NECROPSY: 07/15/86 10:44 PROSECTOR: BARBARA DAY
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP

DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
TERMINAL BODY WEIGHT: 262.0 GRAMS
RECORDED: SID JONES, DVM, PHD, DACUP
WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

HISTOPATHOLOGY

^COLLECTED/TAKEN (XW) :

-ELECTRON MICROSCOPY SAMPLE; LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

LIVER (LD) :

-FOCI OF MODERATE FAT CELLS,-MINIMAL

LUNG (LD) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

PARATHYROID (PT) :

>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), RIB, FEMUR (FF), RIB, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), RIB, FEMUR (FF), RIB, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK),
STOMACH, GL (ST), STOMACH, MINGL (SI), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08390

SEX: FEMALE

DOSE GROUP: 1

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/15/86

STUDY DAY OF DEATH: 96

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 261.7 GRAMS

DATE AND TIME OF NECROPSY: 07/15/86 8:45

PROSECTOR: BARBARA DAY

REFEROR: SID JONES, DVM, PHD, DACVP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DVM, PHD, DACVP

WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.055	.0210 %	.0228	WEIGHT TAKEN
OVARY (OU)	.183	.0699 %	.0925	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.98	.756 %	1.800	WEIGHT TAKEN
HEART (HT)	.77	.296 %	.391	WEIGHT TAKEN
SPLEEN (SP)	.65	.250 %	.330	WEIGHT TAKEN
KIDNEY (KD)	1.78	.680 %	.908	WEIGHT TAKEN
LIVER (LI)	2.07	2.700 %	3.572	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	EYE (EY) : -CHRONIC INFLAMMATION, HARDERIAN GLAND, MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID, -SLIGHT

APPENDIX B

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 296

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 9399188

ANIMAL NUMBER: B08390 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 261.7 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:45 PROSECTOR: BARBARA DAY REFERRED: SID JONES, DUM, PHD, DATUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DATUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD), LATERAL GI, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SP), STOMACH, GI (ST), STOMACH, NINGEL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD), LATERAL GI, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGEL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

STUDY NUMBER: 2399100

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808391 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 277.8 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 14:50 PROSECTOR: TIM GROVE RECORDED: SID JONES, DUM, PHD, DBCUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DBCUP WEIGHT: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS	WEIGHT TAKEN
ADRENAL (AD)	.064	.0231 %	.0349		WEIGHT TAKEN
OVARY (OV)	.106	.0382 %	.0576		WEIGHT TAKEN
BRAIN W/STEM (BR)	1.84	.662 %	1.880		WEIGHT TAKEN
HEART (HT)	.79	.284 %	.429		WEIGHT TAKEN
SPLEEN (SP)	.51	.184 %	.277		WEIGHT TAKEN
KIDNEY (KD)	1.74	.626 %	.946		WEIGHT TAKEN
LIVER (LI)	7.47	2.689 %	4.060		WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

UTERUS (UT) :
-LUMEN, FLUID; BOTH HORNES, CLEAR
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL PRESERVATIONS:NONE

LIVER (LI) :
-FIND OF MODERATE CELLULARITY, MINIMAL
LUNG (LI) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
ITERIS (HI) :
-DILATATION, -MODERATE

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08391 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SACRIFICED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 222.8 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 14:50 PROSECTOR: TIM GRUBB RECIPIENT: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: TIM GRUBB

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UNIDENTIFIED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUED ***

ANIMAL NUMBER: B08392 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 14 TERMINAL BODY WEIGHT: 294.7 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:27 PROSECTOR: BARBARA DAY REFERRED: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

HISTOPATHOLOGY

COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL PRESERVATIONS:NONE
LIVER (LI) :
-FOCI OF MURDERER CELLS,-MINIMAL
LUNG (LU) :
-PERIPHERAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LU), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXN (EX),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (GT), STOMACH, NONE (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LU), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXN (EX),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONE (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED FOR THE STUDY PROTOCOL) WERE OBTAINED ***

ANIMAL NUMBER: B08393

SEX: FEMALE

DISE GROUP: 1

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/16/86

STUDY DAY OF DEATH: 97

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 266.0 GRAMS

DATE AND TIME OF NECROPSY: 07/16/86 10:35

PROSECTOR: DONALD AS HERNIMIN

REQUIRE: STD JIFES, DUM, PHO, DACUP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHO, DACUP

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	^COLLECTED/TAKEN (XU) : -ELECTRON MICROSCOPY SAMPLE: LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LIVER (LI) : -FOCI OF MINOR INFAR CELLS,-MINIMAL LUNG (LU) : -PNEUMONIC/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT PARATHYROID (PT) : >SECTION EXAMINED; TISSUE NOT PRESENT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MENGI (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)		
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MENOLF, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)		

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN S T A T I S T I C S
ADRENAL (AD)	.075	.0311 %	.0349	WEIGHT TAKEN
OVARY (OV)	.136	.0560 %	.0630	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.16	.890 %	1.000	WEIGHT TAKEN
HEART (HT)	.88	.363 %	.408	WEIGHT TAKEN
SPLEEN (SP)	.52	.214 %	.241	WEIGHT TAKEN
KIDNEY (KD)	1.92	.791 %	.889	WEIGHT TAKEN
LIVER (LI)	7.15	2.948 %	3.315	WEIGHT TAKEN

CLINICAL OBSERVATIONS	P A T H O L O G Y O B S E R V A T I O N S	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LIVER (LI) : -FOCI OF MONONUCLEAR CELLS,-MINIMAL FIBROSIS (LI) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT -PNEUMONITIS,-SLIGHT PARATHYROID (PT) : >SECTION EXAMINED: TISSUE NOT PRESENT

APPENDIX B

*** PATH/TOX SYSTEM INPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 302

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08394 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED; TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 242.5 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 13:51 PROSECTOR: DONIGLAS HERNDON RETAINER: SID JONES, DUM, PHD, DAEUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DAEUP WEIGHTER: DONIGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), RINE, FEMUR (FF), RINE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD), LADRIAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNCOLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), RINE, FEMUR (FF), RINE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD), LADRIAL GL, EXO (ED),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2499188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08395 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 269.5 GRAMS
 DATE AND TIME OF NECROPSY: 07/15/86 14:36 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DVM, PhD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACUP WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	O R G A N	
				S T A T U S	W E I G H T T A K E N
ADRENAL (AD)	.091	.0337 %	.0435		WEIGHT TAKEN
OVARY (OU)	.138	.0512 %	.0660		WEIGHT TAKEN
BRAIN W/STEM (BR)	2.09	.776 %	1.0000		WEIGHT TAKEN
HEART (HT)	.81	.301 %	.388		WEIGHT TAKEN
SPLEEN (SP)	.53	.197 %	.254		WEIGHT TAKEN
KIDNEY (KD)	2.16	.801 %	1.033		WEIGHT TAKEN
LIVER (LI)	11.81	4.382 %	5.651		WEIGHT TAKEN

P A T H O L O G Y O B S E R V A T I O N S
 NECROPSY

CLINICAL OBSERVATIONS

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS: NONE

LIVER (LI) :

-FACI OF PORTAL TRACTS, MINIMAL

LUNG (LU) :

-PERIPHERAL PULMONARY, INFILTRATION, LYMPHOCYTES, MINIMAL
 -PNEUMONITIS, MINIMAL

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DEPARTMENT OF PATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 314

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399104

ANIMAL NUMBER: 808395 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 269.5 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 14:36 PROSECUTOR: BARBARA DAY REFUSER: SID JONES, DVM, PhD, DATUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DATUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BLNF, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNIDENTIFIED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BLNF, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808396

SEX: FEMALE

DOSE GROUP: 1

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/15/86

STUDY DAY OF DEATH: 96

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 248.6 GRAMS

DATE AND TIME OF NECROPSY: 07/15/86 15:11

PROSECTOR: DOUGLAS HERNDON

REORDER: SID JONES, DUM, PHD, DACUP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.069	.0276 %	.0368	WEIGHT TAKEN
OVARY (OU)	.141	.0568 %	.0257	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.87	.750 %	1.000	WEIGHT TAKEN
HEART (HT)	.97	.398 %	.519	WEIGHT TAKEN
SPLEEN (SP)	.50	.201 %	.268	WEIGHT TAKEN
KIDNEY (KD)	1.90	.764 %	1.019	WEIGHT TAKEN
LIVER (LT)	8.58	3.450 %	4.598	WEIGHT TAKEN

CLINICAL OBSERVATIONS

APPEARED NORMAL

PATHOLOGY OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

TIME (DD) :

-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, SLIGHT

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 306

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2299108

ANIMAL NUMBER: 808396
SEX: FEMALE
DATE OF DEATH: 07/15/86
STUDY DAY OF DEATH: 96
DATE AND TIME OF NECROPSY: 07/15/86 15:11
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL

DOSE GROUP: 1
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 248.6 GRAMS
PROSECUTOR: DOUGLAS HERNDON
RECORDED: SID JONES, DUM, PHD, DACUP
PATHOLOGIST: SID JONES, DUM, PHD, DACUP
WEIGHER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LABRIMAL GL, EXO (FI),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGEL (SD),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UTERUS (UT), UTERUS (UT), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LABRIMAL GL, EXO (FI),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGEL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 279910R

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08397 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 271.1 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 9:14 PROSECTOR: TIM GROVE REORDER: SID JONES, DVM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.062	.0229 %	.0335	WEIGHT TAKEN
OVARY (OV)	.112	.0413 %	.0605	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.85	.682 %	1.000	WEIGHT TAKEN
HEART (HT)	.78	.288 %	.492	WEIGHT TAKEN
SPLEEN (SP)	.47	.173 %	.254	WEIGHT TAKEN
KIDNEY (KD)	1.85	.682 %	1.000	WEIGHT TAKEN
LIVER (LT)	6.55	2.416 %	3.541	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

KIDNEY (KD) :
 -H-PELVIS, DILATED; RIGHT, SLIGHTLY
 GENERAL INFORMATION (XX) :
 >NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
 -NEPHROPATHY, CHRONIC PROGRESSIVE, -
 MINIMAL
 -PELVIS, DILATATION, -SLIGHT
 LUNG (LL) :
 -PERIBRONCHIAL/PERIVASCULAR,
 INFILTRATION, LYMPHOID, -SLIGHT
 PARATHYROID (PT) :
 >SECTION EXAMINED; TISSUE NOT PRESENT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 308

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08397 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 271.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:14 PROSECTOR: TIM GROVE REFERRED: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2199108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08398 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 225.8 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 13:47 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.045	.0288 %	.0732	WEIGHT TAKEN
OVARY (OU)	.131	.0580 %	.0668	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.96	.868 %	1.0000	WEIGHT TAKEN
HEART (HT)	.68	.301 %	.342	WEIGHT TAKEN
SPLEEN (SP)	.50	.221 %	.255	WEIGHT TAKEN
KIDNEY (KD)	1.58	.700 %	.806	WEIGHT TAKEN
LIVER (LI)	5.33	2.360 %	2.719	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

CLINICAL OBSERVATIONS

HISTOPATHOLOGY

-APPEARED NORMAL

CECUM (CF) :
 -DARK AREA; IN WALL, TUE, RED, 5 X 4 MM

>NOTE>>DARK AREA, POSSIBLE INFECTION SITE

GENERAL INFORMATION (XX) :

>NOTE>>EXTERNAL OBSERVATIONS:NONE

CECUM (CF) :
 -INFECTION SITE,-PRESENT
 LUNG (LU) :
 -PERIBRONCHIAL/PERIVASCULAR,
 INFILTRATION, LYMPHOID,-SLIGHT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 310

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2392100

ANIMAL NUMBER: B08398 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SACRIFICED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 225.8 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 13:47 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DVM, PhD, DACVP REFERRED: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LABRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), THYROID (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), COLLECTED/TAKEN (XL)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LABRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (NU), THYROID (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08399
SEX: FEMALE
DOSE GROUP: 1
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86
STUDY DAY OF DEATH: 97
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 298.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:02
PROSECTOR: BARBARA DAY
RECORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: SID JONES, DVM, PHD, DACVP
WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.083	.0286 %	.0403	WEIGHT TAKEN
OVARY (OV)	.125	.0431 %	.0607	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.86	.710 %	1.000	WEIGHT TAKEN
HEART (HT)	.87	.300 %	.422	WEIGHT TAKEN
SPLEEN (SP)	.58	.200 %	.282	WEIGHT TAKEN
KIDNEY (KD)	1.82	.627 %	.883	WEIGHT TAKEN
LIVER (LI)	7.13	2.458 %	3.461	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID,-SLIGHT -PNEUMONITIS,-SLIGHT

APPENDIX B

*** PATH/TOX SYSTEM TRITUPIT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 312

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808399 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHMIDT, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 290.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 14:02 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DVM, PhD, DACUP MEASUREMENTS: SID JONES, DVM, PhD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACUP MEASUREMENTS: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGA (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT), VENTRICLES/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIA, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (NU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT STUDY NUMBER: 2399108

ANIMAL NUMBER: B08400 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 240.3 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 14:39 PROSECTOR: BARBARA DAY REORDER: SID JONES, DVM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHT: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.084	.0338 %	.0431	WEIGHT TAKEN
OVARY (OV)	.142	.0572 %	.0728	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.95	.785 %	1.000	WEIGHT TAKEN
HEART (HT)	.91	.366 %	.467	WEIGHT TAKEN
SPLEEN (SP)	.55	.222 %	.282	WEIGHT TAKEN
KIDNEY (KD)	1.90	.765 %	.974	WEIGHT TAKEN
LIVER (LI)	8.30	3.343 %	4.256	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

UTERUS (UT) :
 -LUMEN, FLUID; BOTH HORNS, CLEAR
 GENERAL INFORMATION (XX) :
 >NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :
 -PERIBRONCHIAL/PERIVASCULAR
 INFILTRATION, LYMPHOID, -SLIGHT
 PARATHYROID (PT) :
 >SECTION EXAMINED; TISSUE NOT PRESENT
 UTERUS (UT) :
 -DILATATION, -MODERATE

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08400 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 248.3 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 14:39 PROSECTOR: BARBARA DAY RETROPER: SID JONES, DUM, FUD, DADUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DADUP WEIGHTER: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (ED),
 LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
 PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SG),
 THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (ED),
 LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
 NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
 STOMACH, GL (ST), STOMACH, NONGL (SG), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B
*** PATH/TOX SYSTEM INPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS
INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTED: 12-MAY-88
PAGE: 315

STUDY NUMBER: 2199100

ANIMAL NUMBER: B08401 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 262.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 15:03 PROSECTOR: DOUGLAS HERNDON RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN SLICES	WEIGHT TAKEN
ADRENAL (AD)	.064	.0245 %			.0328
OVARY (OV)	.114	.0436 %			.0584
BRAIN W/STEM (BR)	1.96	.747 %			1.000
HEART (HT)	.91	.345 %			.462
SPLEEN (SP)	.50	.189 %			.253
KIDNEY (KD)	2.10	.802 %			1.074
LIVER (LI)	8.32	3.173 %			4.249

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LL) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
PARATHYROID (PT) :
>SECTION EXAMINED; TISSUE NOT PRESENT
UTERUS (UT) :
-OVARITIS, -SLIGHT

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 316

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08401 SEX: FEMALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 262.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 15:03 PROSECTOR: DOUGLAS HERNDON RECTOR: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXN (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNIDENTIFIED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXN (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808422 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 260.3 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 10:00 PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MUSEL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 318

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08423 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 259.0 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 11:15 PROSECTOR: DOUGLAS HERFORD REORDER: SID JONES, DUM, PHD, DADUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DADUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS,-MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LADRIAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEN (SP), STOMACH, ST (ST), STOMACH, NONS (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08424

SEX: FEMALE

DOSE GROUP: 2

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 14

TERMINAL BODY WEIGHT: 272.9 GRAMS

DATE AND TIME OF NECROPSY: 07/14/86 14:00

PROSECTOR: DOUGLAS HERNDON

RECORDER: SID JONES, DVM, PHD, DACUP

POST-FIX METHOD: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DVM, PHD, DACUP

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
<div> <div>APPEARED NORMAL</div> <div> <div>^COLLECTED/TAKEN (XN) :</div> <div>-ELECTRON MICROSCOPY SAMPLE ; LIVER</div> <div>GENERAL INFORMATION (XX) :</div> <div>>NOTE:>>EXTERNAL OBSERVATIONS:NONE</div> </div> </div>	<div> <div>LIVER (LI) :</div> <div>-FOCUS OF MINIMAL INFLAMMATION, MINIMAL</div> <div>LUNG (LU) :</div> <div>-PERIBRONCHIAL/PERIVASCULAR,</div> <div>INFILTRATION, LYMPHOID,-SLIGHT</div> </div>

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EX),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NORMAL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08425 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 261.3 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 9:45 PROSECTOR: TIM GROVE RECIPIER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.060	.0230 %	.0326	WEIGHT TAKEN
OVARY (OU)	.116	.0444 %	.0630	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.84	.704 %	1.000	WEIGHT TAKEN
HEART (HT)	.90	.344 %	.489	WEIGHT TAKEN
SPLEEN (SP)	.51	.195 %	.277	WEIGHT TAKEN
KIDNEY (KO)	1.80	.689 %	.978	WEIGHT TAKEN
LIVER (LI)	10.14	3.881 %	5.511	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :
-PERITONEAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THYROID (AD), BLADDER, FEMUR (FE), BLADDER, SUPRACRURAL (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KO), LATERAL BL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GI (ST), STOMACH, NINEL (SD),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), COLLECTED-TAKEN (XD)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08426 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 236.1 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 14:33 PROSECTOR: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), COLON (CO), CORD, FRONTAL (FS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL., EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SO), SPICTR (SP), STOMACH, IN (SI), STOMACH, MURK (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 372

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08427 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 225.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 12:56 PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	O R G A N	
				S T A T U S	
ADRENAL (AD)	.053	.0194 %	.0289	WEIGHT TAKEN	
OVARY (OU)	.110	.0401 %	.0526	WEIGHT TAKEN	
BRAIN W/STEM (BR)	1.85	.673 %	1.000	WEIGHT TAKEN	
HEART (HT)	.88	.321 %	.478	WEIGHT TAKEN	
SPLEEN (SP)	.68	.248 %	.369	WEIGHT TAKEN	
KIDNEY (KD)	1.81	.659 %	.929	WEIGHT TAKEN	
LIVER (LI)	7.70	2.798 %	4.157	WEIGHT TAKEN	

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LD) :

-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID, MINIMAL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), PINE, FEMUR (FE), RIB, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JJ), KIDNEY (KD), PANTHRA (PT), EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAJOR SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NORMAL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UU), VAGINA/TAKEN (XN)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 219914R

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08428
SEX: FEMALE
DOSE GROUP: 2
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86
STUDY DAY OF DEATH: 96
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 275.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 8:35
PROSECTOR: TIM GROVE
REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: SID JONES, DUM, PHD, DACUP
WEIGHER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN TO STOMACH WEIGHT RATIO
ADRENAL (AD)	.067	.0245 %	.0363	WEIGHT TAKEN
OVARY (OU)	.123	.0445 %	.0661	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.86	.673 %	1.000	WEIGHT TAKEN
HEART (HT)	.88	.321 %	.476	WEIGHT TAKEN
SPLEEN (SP)	.50	.181 %	.268	WEIGHT TAKEN
KIDNEY (KD)	1.54	.558 %	.879	WEIGHT TAKEN
LIVER (LI)	6.09	2.207 %	3.278	WEIGHT TAKEN

CLINICAL OBSERVATIONS
-APPEARED NORMAL
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR, INFLTRATION, LYMPHOID, SLIGHT
HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORATIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, FSD (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MNGS (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VAGINA/TAKEN (VM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE HARVESTED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 324

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 9399188

ANIMAL NUMBER: B08429 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 286.6 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 15:04 PROSECUTOR: BARBARA DAY REFERRED: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHT: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.073	.0255 %	.0351	WEIGHT TAKEN
OVARY (OV)	.160	.0558 %	.0769	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.08	.726 %	1.808	WEIGHT TAKEN
HEART (HT)	.88	.307 %	.423	WEIGHT TAKEN
SPLEEN (SP)	.73	.255 %	.351	WEIGHT TAKEN
KIDNEY (KD)	2.27	.792 %	1.091	WEIGHT TAKEN
LIVER (LI)	7.80	2.722 %	3.258	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

KIDNEY (KD) :
-PELVIS, DILATED; RIGHT, MODERATELY;
LEFT, SLIGHTLY
UTERUS (UT) :
-LUMEN, FLUID; BOTH HORNS, CLEAR
GENERAL INFORMATION (XX) :
>NOTE:>>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-PELVIS, DILATED, -SLIGHT
LIVER (LI) :
-FACI OF MODIFIED FAT CELLS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
-PNEUMONITIS, -MINIMAL
UTERUS (UT) :
-DILATION, -MODERATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CEREBRAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JJ), LACRIMAL GL, EXO (EG), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (MS), MANDIB, STERNUM (SI),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, BL (ST), SURGICAL, NERVE (SD), THYROID (TH), UTERUS (UT),
TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS

STUDY NUMBER: 2392188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08430 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SACRIFICED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 229.7 GRAMS
 DATE AND TIME OF NECROPSY: 07/15/86 14:45 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.075	.0325 %	.0327	WEIGHT TAKEN
OVARY (OU)	.108	.0469 %	.0544	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.98	.862 %	1.000	WEIGHT TAKEN
HEART (HT)	.84	.367 %	.426	WEIGHT TAKEN
SPLEEN (SP)	.51	.224 %	.259	WEIGHT TAKEN
KIDNEY (KD)	1.94	.847 %	.982	WEIGHT TAKEN
LIVER (LI)	8.55	3.724 %	4.319	WEIGHT TAKEN

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS HISTOPATHOLOGY
 -APPEARED NORMAL GENERAL INFORMATION (XX) : LUNG (LU) :
>NOTE:>EXTERNAL OBSERVATIONS: NONE - PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
 ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CEREBRAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (ED),
 LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
 PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONE (SL),
 THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
 KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

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DEPARTMENT OF PATHOLOGY

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-81
PAGE: 326

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: 808431 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCINFIRMED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 252.3 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 9:24 PROSECTOR: BARBARA DAY REFORMER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

MAMMARY GLAND (MG) :

-MASS-UFL; LEFT AXILLA, ONE, SEMI-FIRM, NODULAR, TAN, RED, 1.8 X 1.6 X 0.6 CM, CUT SURFACE: SAME

COLLECTED/TAKEN (XLM) :

-ELECTRON MICROSCOPY SAMPLE; LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:MASS-UFL

IN CAPSULE #1

GENERAL INFORMATION :

>TISSUE MASS:> #1; 1.0640 GRAMS; UFL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), DUOD, CERVICAL (CS), DUOD, HUMER (HU), CIRC, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LADRIAL GL, EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAID SALIVARY GL (SG), MARIUM, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808432 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 TERMINAL BODY WEIGHT: 254.6 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:38 PROSECUTOR: TIM GROVE RECORDER: SID JONES, DCM, PhD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DCM, PhD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.057	.0224 %	.0315	WEIGHT TAKEN
OVARY (OU)	.112	.0440 %	.0619	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.81	.711 %	1.688	WEIGHT TAKEN
HEART (HT)	.75	.295 %	.414	WEIGHT TAKEN
SPLEEN (SP)	.51	.200 %	.282	WEIGHT TAKEN
KIDNEY (KD)	1.60	.628 %	.884	WEIGHT TAKEN
LIVER (LI)	6.00	2.357 %	3.315	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS
-APPEARED NORMAL
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE
NECROPSY
HISTOPATHOLOGY
KIDNEY (KO) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELTAL (SM), NERVE, SCROTIC (SR), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINOR (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VESICULAE/TAKEN (VJ)

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 328

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08433 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 265.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 10:52 PROSECTOR: TIM GROVE REORDER: STD JONES, DUM, PHO, DADUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHO, DADUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XU) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CARD, CERVICAL (CS), CARD, LUMBAR (LC), CORIO, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIGEE (SP), STOMACH, G (ST), STOMACH, MARS (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

PRINTED: 12-MAY-86
PAGE: 329

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08434 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHENKED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 243.1 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:38 PROSECTOR: TIM GROVE PATHOLOGIST: SID JONES, DVM, PhD, DACUP REORDER: SID JONES, DVM, PhD, DACUP
POST-FTX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -S LIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, BL (ST), STOMACH, INTRA (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2397188

ANIMAL NUMBER: B08435 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 241.5 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 13:48 PROSECUTOR: TIM GROVE RECORDED: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACVP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	STATUS
ADRENAL (AD)	.078	.0323 %	.0386	WEIGHT TAKEN
OVARY (OU)	.106	.0439 %	.0525	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.02	.836 %	1.000	WEIGHT TAKEN
HEART (HT)	.79	.327 %	.391	WEIGHT TAKEN
SPLEEN (SP)	.42	.174 %	.208	WEIGHT TAKEN
KIDNEY (KO)	1.96	.812 %	.970	WEIGHT TAKEN
LIVER (LI)	7.76	3.213 %	3.842	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

KIDNEY (KO):
-PELVIS, DILATED; RIGHT, MODERATELY
GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERVATIONS: NONE

HISTOPATHOLOGY

KIDNEY (KO):
-NEPHROPATHY, CHRONIC PRESSURE,
MINIMAL
-PELVIS, DILATION, -MODERATE
LUNG (LU):
-PERICARDIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JJ), LACRIMAL GL, EXO (EG), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SD), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VULVA (V), COLLECTED/TAKEN (XAL)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
LIVER (LI)

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808436 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHUBERD, TERMINAL SACRIFICE

DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 14 TERMINAL BODY WEIGHT: 252.5 GRAMS

DATE AND TIME OF NECROPSY: 07/16/86 14:16 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DVM, PhD, DACVP

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.063	.0245 %	.0317	WEIGHT TAKEN
OVARY (OV)	.087	.0338 %	.0437	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.99	.773 %	1.000	WEIGHT TAKEN
HEART (HT)	.78	.303 %	.392	WEIGHT TAKEN
SPLEEN (SP)	.52	.202 %	.261	WEIGHT TAKEN
KIDNEY (KD)	1.78	.691 %	.894	WEIGHT TAKEN
LIVER (LI)	7.25	2.816 %	3.643	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BLIND, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAJOR SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELTAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), STOMACH (ST), STOMACH, GL (ST), STOMACH, MURIAL (SM),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VULVA/TAKEN (VX)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAID ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 739910A

ANIMAL NUMBER: B08437 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 243.2 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 12:15 PROSECTOR: TIM GROVE
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

NECROPSY

HISTOPATHOLOGY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :

-ELECTRON MICROSCOPY SAMPLE: LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KD) :

-PELVIS, DILATATION,-SLIGHT

LIVER (LI) :

-PECT OF MORPHOLOGY FOR EFFUS,-MINIMAL

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINOR (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 333

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808438 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 277.4 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:12 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHO, DAIJUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHO, DAIJUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, -SLIGHT
LUNGS (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CERO, LUMBAR (LC), CORO, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAID SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SH), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SP), STOMACH, SI (SI), STOMACH, NONEN (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86
PAGE: 314

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: 808439 SEX: FEMALE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97
DATE AND TIME OF NECROPSY: 07/16/86 10:50 PROSECTOR: BARBARA DAY
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
TERMINAL BODY WEIGHT: 261.4 GRAMS
REORDER: SID JONES, DVM, PhD, DACVP
WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAID SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEN (SS), STOMACH, SI (ST), STOMACH, HONG (SH),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08440 SEX: FEMALE DISE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 253.9 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 14:38 PRISECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.076	.0298 %	.0386	WEIGHT TAKEN
OVARY (OV)	.121	.0477 %	.0618	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.96	.771 %	1.000	WEIGHT TAKEN
HEART (HT)	.86	.338 %	.438	WEIGHT TAKEN
SPLFEN (SP)	.60	.238 %	.309	WEIGHT TAKEN
KIDNEY (KD)	1.83	.719 %	.933	WEIGHT TAKEN
LIVER (LI)	8.05	3.169 %	4.112	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :
 >NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG (LI) :
 -PERIPHERAL/PERIVASCULAR INFILTRATION, LYMPHOID, -SIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), PINE, FEMUR (FE), RIB, STERNUM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), LIFIM (LI), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXN (EX), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (SL), STOMACH, NIBEL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VAGINATED/TAKEN (VM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 336

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08441 SEX: FEMALE DOSE GROUP: 2 SACRIFICE STATUS: SCHMIDT, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 254.6 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 15:06 PROSECTOR: TIM GRINE REFERRED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: TIM GRINE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS	WEIGHT TAKEN
ADRENAL (AD)	.077	.0382 %	.0393		WEIGHT TAKEN
OVARY (OV)	.108	.0424 %	.0551		WEIGHT TAKEN
BRAIN W/STEM (BR)	1.96	.770 %	1.0000		WEIGHT TAKEN
HEART (HT)	.89	.350 %	.454		WEIGHT TAKEN
SPLEEN (SP)	.40	.157 %	.204		WEIGHT TAKEN
KIDNEY (KD)	1.88	.738 %	.959		WEIGHT TAKEN
LIVER (LI)	8.50	3.339 %	4.332		WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE: EXTERNAL OBSERVATIONS: NONE

LIVER (LI) :

-FIELD OF MICROSCOPIC CELLS: MINIMAL

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID; SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SP), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CEREBRAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JJ), KIDNEY (KD), LACRIMAL GL, EXU (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIRTER (SP), STOMACH, BL (SL), STOMACH, HESL (SH), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808462

SEX: FEMALE

DOSE GROUP: 3

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 14

TERMINAL BODY WEIGHT: 247.8 GRAMS

DATE AND TIME OF NECROPSY: 07/14/86 10:29

PROSECTOR: BARBARA DAY

REFERENCE: SID JONES, DUM, PHD, DACUP

POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		
CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : >NOTE:>>EXTERNAL OBSERVATIONS:NONE	LUNGS (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAID SALIVARY GL (SG),

MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),

PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, SI (SI), STOMACH, NINEAL (SN),

THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-80
PAGE: 338

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08463 SEX: FEMALE DISE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 236.6 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 10:09 PROSECTOR: BARBARA DAY REFUSER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.075	.0317 %	.0383	WEIGHT TAKEN
OVARY (OU)	.116	.0489 %	.0591	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.96	.827 %	1.000	WEIGHT TAKEN
HEART (HT)	.80	.338 %	.408	WEIGHT TAKEN
SPLEEN (SP)	.55	.234 %	.283	WEIGHT TAKEN
KIDNEY (KO)	1.73	.733 %	.886	WEIGHT TAKEN
LIVER (LI)	8.95	3.783 %	4.574	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS: NONE

LUNG (LU) :

-PULMONARY PERIVASCULAR INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BLADDER, FEMUR (FF), HEART, STERNUM (SS), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LO), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KO), LACRIMAL GL, FOX (FD), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, BL (ST), STOMACH, MINOR (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VAGINA (VA)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08464 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 239.5 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:37 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DUM, PHD, DAIJUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DAIJUP WEIGHT: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.069	.0287 %	.0347	WEIGHT TAKEN
OVARY (OU)	.116	.0484 %	.0584	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.98	.828 %	1.000	WEIGHT TAKEN
HEART (HT)	.78	.325 %	.393	WEIGHT TAKEN
SPLEEN (SP)	.39	.161 %	.195	WEIGHT TAKEN
KIDNEY (KO)	1.78	.743 %	.897	WEIGHT TAKEN
LIVER (LI)	7.95	3.320 %	4.011	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERVATIONS:NONE

TISS (UU):
-PERIBRONCHIAL/PERIVASCULAR,
PERITREATMENT, LYMPHATIC, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), SPINE, FEMUR (FF), HONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SD), Ovary (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MUSCLE (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNIDENTIFIED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399180

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808465 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 249.3 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:58 PROSECUTOR: TIM GROVE RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.054	.0217 %	.0287	WEIGHT TAKEN
OVARY (OU)	.126	.0505 %	.0668	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.98	.796 %	1.800	WEIGHT TAKEN
HEART (HT)	.79	.318 %	.421	WEIGHT TAKEN
SPLEEN (SP)	.50	.201 %	.267	WEIGHT TAKEN
KIDNEY (KD)	2.14	.858 %	1.135	WEIGHT TAKEN
LIVER (LI)	6.05	2.429 %	3.214	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	UTERUS (UT) : -LUMEN, FLUID; BOTH HORNS, CLEAR GENERAL INFORMATION (XX) : >NOTE>EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID, -MINIMAL INTERST (IT) : -DILATATION, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KD), LIVER (LI), LUNG (LU), MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANTHERS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MURAL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ADULTIFIED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808466 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: RESCHEDULED (R)
DATE OF DEATH: 07/07/86 STUDY WEEK OF DEATH: 13 TERMINAL BODY WEIGHT: 280.5 GRAMS
DATE AND TIME OF NECROPSY: 07/07/86 14:58 PROSECTOR: BARBARA DAY RECORDED BY: BARBARA DAY
POST-FTX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

HISTOPATHOLOGY

LUNG (LH) :

-FAILURE TO COLLAPSE; ALL LUNGES
-MOTTLED; ALL LOBES, LIGHT TO DARK RED
GENERAL INFORMATION (XXX) :

>NOTE:>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS:NONE. FOUND DEAD AT
ONE HOUR POST-DOSE OBSERVATIONS

LUNG (LH) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT
-FOREIGN MATERIAL,-PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), FEMUR (FE), FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXN (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF),
MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONEL (SU), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), FEMUR (FE), FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXN (ED),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONEL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 142

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2199108

ANIMAL NUMBER: B08467 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 TERMINAL BODY WEIGHT: 252.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 11:29 PROSECTOR: BARBARA DAY RECORDED: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

HISTOPATHOLOGY

COLLECTED/TAKEN (XM) : KIDNEY (KD) :
-ELECTRON MICROSCOPY SAMPLE; LIVER -NEPHROPATHY, CHRONIC PROGRESSIVE,
GENERAL INFORMATION (XX) : MINIMAL
>NOTE:>EXTERNAL OBSERVATIONS:NONE LUNG (LD) :
-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SH), OVARY (OV), PANCREAS (PA), PNEUMONIA (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MURDER (UR),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08468 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: UNSPECIFIED (N)
DATE OF DEATH: 04/28/86 STUDY DAY OF DEATH: 18 STUDY WEEK OF DEATH: 3 TERMINAL BODY WEIGHT: 201.3 GRAMS
DATE AND TIME OF NECROPSY: 04/28/86 15:33 PROSECTOR: BARBARA DAY REFERRED: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

LUNG (LU) :

-FAILURE TO COLLAPSE; ALL LOBES
-MOTTLED; ALL LOBES, LIGHT TO DARK RED
GENERAL INFORMATION (XX) :
>NOTE:>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS:NONE. DIED WITHIN
ONE HOUR OF DOSSING

HISTOPATHOLOGY

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID, -SLIGHT
-FIBROUS MATERIAL, -PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MANDIB, STERNUM (SF),
MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MAND (MD), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), *COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, MAND (MD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 144

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08469 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 258.1 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 14:21 PROSECUTOR: TIM GROVE REFERRED: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XII) :
-ELECTRIN MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-HEPATOPLATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LIVER (LI) :
-FOCI OF MINIMINUCLEAR CELLS, -MINIMAL
LUNG (LU) :
-PERITONIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LO), CORD, SACRATIC (SC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (CS), SPLEEN (SP), STOMACH, SI (SI), STOMACH, NINE (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808470	SEX: FEMALE	DOSE GROUP: 3	SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86	STUDY DAY OF DEATH: 96	STUDY WEEK OF DEATH: 14	TERMINAL BODY WEIGHT: 236.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 9:32	PROSECTOR: TIM GROVE		RECIPIENT: SID JONES, DUM, PHD, DADUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL	PATHOLOGIST: SID JONES, DUM, PHD, DADUP	WEIGHER: TIM GROVE	
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO
ADRENAL (AD)	.058	.0246 %	.0313
OVARY (OV)	.108	.0457 %	.0581
BRAIN W/STEM (BR)	1.86	.786 %	1.000
HEART (HT)	.78	.329 %	.418
SPLEEN (SP)	.62	.260 %	.331
KIDNEY (KD)	1.71	.723 %	.919
LIVER (LI)	6.47	2.733 %	3.475

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNG (UU) : -PERICARDIAL/PERIVASCULAR INFILTRATION, LYMPHOID, SLIGHT
<p>THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:</p> <p>ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), RIBS, FEMUR (FF), RIBS, STERNUM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), JEJUNUM (JE), KIDNEY (KO), LIVER (LI), EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), PANCREAS (PA), PARATHYROID (PT), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PAROTID (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NERVE (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), COLLECTED/TAKEN (XU)</p> <p>THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:</p> <p>KIDNEY (KD), LIVER (LI)</p>		

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B
 *** PATH/TOX SYSTEM OUTPUT ***
 SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDUAL ANIMAL SUMMARY REPORT STUDY NUMBER: 2399108

ANIMAL NUMBER: 808471 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: EUTHANIZED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 249.4 GRAMS
 DATE AND TIME OF NECROPSY: 07/15/86 14:20 PRETREATMENT: BARBARA DAY RETENDER: SID JONES, DVM, PhD, DACVP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.086	.0345 %	.0462	WEIGHT TAKEN
OVARY (OV)	.140	.0560 %	.0751	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.86	.746 %	1.000	WEIGHT TAKEN
HEART (HT)	.94	.377 %	.505	WEIGHT TAKEN
SPLEEN (SP)	.68	.273 %	.366	WEIGHT TAKEN
KIDNEY (KD)	1.99	.798 %	1.070	WEIGHT TAKEN
LIVER (LI)	10.57	4.239 %	5.684	WEIGHT TAKEN

CLINICAL OBSERVATIONS PATHOLOGY OBSERVATIONS

-APPEARED NORMAL
 GENERAL INFORMATION (XX) :
 >NOTE:>EXTERNAL OBSERVATIONS:NONE
 KIDNEY (KD) :
 MINIMAL
 LIVER (LI) :
 -FACI HC MEASURED FOR LELLS.-MINIMAL
 LUNG (LU) :
 -PERIBRONCHIAL/PERIVASCULAR,
 INFILTRATION, LYMPHOID,-SLIGHT

HISTOPATHOLOGY
 THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
 ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CIRC, UTERUS (UT), CIRC, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (ED),
 LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MANTARY GLAND (MG), MANDIBULAR GL (MG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
 PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NODUS (SD),
 THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), COLLECTED/TAKEN (XU)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808472 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 298.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:38 PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DUM, PhD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PhD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE: LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LIVER (LI) : -FOOT OF MINOR FOCAL CELLS,-MINIMAL LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: ADRENAL, CORTX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERO, CERVICAL (CS), CERO, LUMBAR (LC), CERO, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, AL (ST), STOMACH, NINGI (SI), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)		
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD)		

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2199108

ANIMAL NUMBER: 808473 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 04/18/86 STUDY WEEK OF DEATH: 2 TERMINAL BODY WEIGHT: 145.7 GRAMS
DATE AND TIME OF NECROPSY: 04/18/86 15:45 PROSECTOR: BARRARA DAY RECORDER: BARRARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

LUNG (LU) :

-FAILURE TO COLLAPSE; ALL LOBES
-MOTTLED; ALL LOBES, LIGHT TO DARK RED
GENERAL INFORMATION (XX) :

>NOTE:>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS:NONE

HISTOPATHOLOGY

BONE, FEMUR (FE) :

-ARTICULAR SURFACE NOT PRESENT, -PRESENT
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
-FOREIGN MATERIAL, -PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), ARTERY, FEMUR (FE), BONE, FEMUR (FB), BONE, FEMUR (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), JEJUNUM (JE), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LT), LN, MESENTERIC (MS), LN, OTHER (LO), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, FEMUR (FB), BONE, FEMUR (SB),
COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY),
HEART (HT), JEJUNUM (JE), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LT), LN, MESENTERIC (MS),
MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN),
OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), STOMACH, GL (ST),
STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08474, SEX: FEMALE, DOSE GROUP: 3, SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86, STUDY DAY OF DEATH: 14, TERMINAL BODY WEIGHT: 249.0 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 9:46, PROSECTOR: BARBARA DAY, RECORDED: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL, PATHOLOGIST: SID JONES, DVM, PhD, DACVP, WETTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LID): -PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CEREBRAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LID), MAMMARY GLAND (MG), MANDIBULAR GL (MG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), OTHER (SS), SPIFF (SP), STOMACH, ST (ST), STOMACH, NIPES (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2199108

ANIMAL NUMBER: B08475 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 258.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:05 PROSECTOR: TIM GROVE REFORDER: SID JONES, DVM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACVP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS	WEIGHT TAKEN
ADRENAL (AD)	.078	.0182 %	.0426		WEIGHT TAKEN
OVARY (OU)	.139	.0339 %	.0760		WEIGHT TAKEN
BRAIN W/STEM (BR)	1.83	.789 %	1.000		WEIGHT TAKEN
HEART (HT)	.78	.302 %	.426		WEIGHT TAKEN
SPLEEN (SP)	.57	.221 %	.311		WEIGHT TAKEN
KIDNEY (KD)	1.85	.717 %	1.011		WEIGHT TAKEN
LIVER (LI)	6.88	2.666 %	3.768		WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

KIDNEY (KD) :

MINIMAL

LIVER (LI) :

-PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID, SLIGHT

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), LIVER (LI), LUNG (LU), THYROID (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXL (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MANDIBULAR GL (MD),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, IN (ST), STOMACH, NODAL (SD),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), *COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATIONS:
LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2799108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08476 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 TERMINAL BODY WEIGHT: 269.2 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 17:06 PROSECTOR: ANUGI AS HERNDON REFERENCE: SID JONES, DUM, PHD, DAIJUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DAIJUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S	
CLINICAL OBSERVATIONS	HISTOPATHOLOGY
- APPEARED NORMAL	
STOMACH, GL (ST) :	LUNG (LH) :
- DARK AREA; FUNDIC MUCOSA, DARK RED	- PERITONEAL / PERIVASCULAR,
UTERUS (UT) :	INFILTRATION, LYMPHOID, -SLIGHT
- LIVER, FLUID; BOTH HORNS, CLEAR	STOMACH, GL (ST) :
- COLLECTED/TAKEN (XW) :	- CONGESTION, -SLIGHT
- ELECTRON MICROSCOPY SAMPLE; LIVER	UTERUS (UT) :
GENERAL INFORMATION (XX) :	- DILATATION, -MODERATE
> NOTE: > EXTERNAL OBSERVATIONS: NONE	

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), CILION (CO), CORD, CERVICAL (CS), CORD, LUMBAR (L), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EX (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAID SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (CS), SPLEN (SP), STOMACH, MINOR (SD), THYMUS (TH),
THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE INREMARKABLE AT MICROSCOPIC EXAMINATION:
KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08477 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 275.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:57 PROSECUTOR: TIM GROVE REFERRED: SID JONES, DUM, PHD, DATUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DATUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLES: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MANDIBULAR GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MUCOSA (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE HARVESTED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 353

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08478
SEX: FEMALE
DATE OF DEATH: 04/20/86
DATE AND TIME OF NECROPSY: 04/20/86 11:35
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL

DOSE GROUP: 3
STUDY WEEK OF DEATH: 2
PROSECTOR: KIM LINCOLN
PATHOLOGIST: NOT REQUIRED BY PROTOCOL

SACRIFICE STATUS: UNSCHEDULED (D)
TERMINAL BODY WEIGHT: 180.2 GRAMS
REFUGER: KIM LINCOLN
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS
NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

LUNG (LU) :
-FAILURE TO COLLAPSE; ALL LOBES, FLUID
FILLED
-MOTTLED; ALL LOBES, LIGHT TO DARK RED
GENERAL INFORMATION (XX) :
>NOTE>LAST IN-LIFE AND EXTERNAL
OBSERVATIONS: NONE. DUSED AT
10:00 AM, FOUND DEAD AT 11:30 AM

HISTOPATHOLOGY

EYE (EY) :
>TISSUE MISSING
>NOTE>SEVERE ARTIFACT PRECLUDE
INTERPRETATION.
KIDNEY (KD) :
-NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
-PELVIS, DILATATION, -MODERATE
LUNG (LU) :
-PNEUMONICAL /PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT
-FOREIGN MATERIAL, -PRESENT
RECTUM (RE) :
>TISSUE MISSING

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 354

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 73991108

ANIMAL NUMBER: B08478 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (U)
DATE OF DEATH: 04/20/86 STUDY DAY OF DEATH: 10 STUDY WEEK OF DEATH: 2 TERMINAL BODY WEIGHT: 180.2 GRAMS
DATE AND TIME OF NECROPSY: 04/20/86 11:35 PROSECTOR: KIM LINDLIN RECORDS: KIM LINDLIN
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHT: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), *COLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808479 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 TERMINAL BODY WEIGHT: 242.1 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:59 PROSECTOR: BARBARA DAY REFERRED BY: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	LUNG (LU) : -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES, LIGHT TO DARK RED GENERAL INFORMATION (XX) : >NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT -FOREIGN MATERIAL,-PRESENT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CIRD, LUMBAR (LO), CIRD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (ON), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIUM, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ^COLLECTED/TAKEN (XU)		
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CIRD, CERVICAL (CS), CIRD, LUMBAR (LO), CIRD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIUM, STERNUM (SE), SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)		

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 356

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08480 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 TERMINAL BODY WEIGHT: 252.7 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:03 PROSECTOR: DOUGLAS HERRON REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

HISTOPATHOLOGY

CLINICAL OBSERVATIONS

NECROPSY

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAJOR SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, ST, STOMACH, MINOR (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

HEART (HT), KIDNEY (KD), LIVER (LI), LUNG (LU)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08481 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 TERMINAL BODY WEIGHT: 259.0 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:41 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LUNG, (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SA),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXD (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GL AND (MG), MAM GLUTARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SI), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, IS (ST), STOMACH, NONES (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

KIDNEY (KO), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08502 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 TERMINAL BODY WEIGHT: 259.9 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 11:11 PROSECTOR: TIM GROVE RECORDED: SID JONES, DUM, PHD, DAIUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DAIUP WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.066	.0254 %	.0354	WEIGHT TAKEN
OVARY (OV)	.096	.0370 %	.0516	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.86	.717 %	1.000	WEIGHT TAKEN
HEART (HT)	.77	.296 %	.413	WEIGHT TAKEN
SPLEEN (SP)	.53	.203 %	.283	WEIGHT TAKEN
KIDNEY (KD)	1.93	.742 %	1.035	WEIGHT TAKEN
LIVER (LI)	7.14	2.747 %	3.830	WEIGHT TAKEN

CLINICAL OBSERVATIONS PATHOLOGY OBSERVATIONS HISTOPATHOLOGY

-APPEARED NORMAL GENERAL INFORMATION (XX) : BONE, FEMUR (FF) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE -ARTICULAR SURFACE NOT PRESENT, -PRESENT
KIDNEY (KD) : -NEPHROPATHY, CHRONIC PROGRESSIVE, -
MINIMAL
LUNG (LU) : -PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID, -SLIGHT
UTERUS (UT) : -DILATION, -SLIGHT

APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 359

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 739910R

ANIMAL NUMBER: B08502 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 259.9 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 11:11 PROSECTOR: TIM GROVE RECORDER: SID JONES, DUM, PHD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACVP WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SNU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ADMITTED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, STERNUM (SB), BRAIN W/STEM (BR), LIVER (LI),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY),
HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SNU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08503

SEX: FEMALE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 95

DATE AND TIME OF NECROPSY: 07/14/86 13:19

STUDY WEEK OF DEATH: 14

POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

PROSECTOR: BARBARA DAY

PATHOLOGIST: SID JONES, DVM, PHD, DACVP

WEIGHER: BARBARA DAY

DOSE GROUP: 4

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

TERMINAL BODY WEIGHT: 235.2 GRAMS

REFORDER: SID JONES, DVM, PHD, DACVP

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATISTICS
ADRENAL (AD)	.061	.0258 %	.0309	WEIGHT TAKEN
OVARY (OU)	.099	.0420 %	.0503	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.96	.835 %	1.000	WEIGHT TAKEN
HEART (HT)	.72	.308 %	.369	WEIGHT TAKEN
SPLEEN (SP)	.50	.214 %	.256	WEIGHT TAKEN
KIDNEY (KD)	1.74	.739 %	.885	WEIGHT TAKEN
LIVER (LI)	6.89	2.931 %	3.510	WEIGHT TAKEN

CLINICAL OBSERVATIONS

APPEARED NORMAL

PATHOLOGY OBSERVATIONS

NETROPSY

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

EYE (EY) :

-CHRONIC INFLAMMATION, HARDERIAN GLAND,- SLIGHT

LUNG (LID) :

-PERIBRONCHIAL/PERIVASCULAR INFILTRATION, LYMPHOID,-SLIGHT

UTERUS (UT) :

-OILATION,-SLIGHT

HISTOPATHOLOGY

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08503
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86
STUDY DAY OF DEATH: 95
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 235.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 13:19
PROSECTOR: BARBARA DAY
RECTOR: SID JONES, DVM, PHD, DACUP
WEIGHER: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SI), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VULVATED/TAKEN (VM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 362

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 7399108

ANIMAL NUMBER: B08504 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 228.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 10:20 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

NECROPSY

HISTOPATHOLOGY

-APPEARED NORMAL

^COLLECTED/TAKEN (XW) :

-ELECTRON MICROSCOPY SAMPLE; LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID, SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (ON), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SO), SPLEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SNL),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), BONE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SNL), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SACED ***

ANIMAL NUMBER: B08505

SEX: FEMALE

DOSF GROUP: 4

SACRIFICE STATUS: UNSCHEDULED (D)

DATE OF DEATH: 04/21/86

STUDY DAY OF DEATH: 11

STUDY WEEK OF DEATH: 2

TERMINAL BODY WEIGHT: 175.2 GRAMS

DATE AND TIME OF NECROPSY: 04/21/86 15:05

PROSECTOR: BARBARA DAY

RECORDER: BARBARA DAY

WEIGHER: NOT REQUIRED BY PROTOCOL

POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: NOT REQUIRED BY PROTOCOL

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	<div> <div>LACRIMAL GL, EXO (EO) :</div> <div>-DARK AREA; 1 LEFT, MULTIPLE, DARK RED, PINPOINT</div> <div>LUNG (LU) :</div> <div>-FAILURE TO COLLAPSE; ALL LOBES</div> <div>-MOTTLED; ALL LOBES, LIGHT TO DARK RED</div> <div>GENERAL INFORMATION (XX) :</div> <div>>NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS: CONVULSIONS, GASPING, DIED AFTER DRUGING GAUZE</div> </div>	<div> <div>ADRENAL, MEDULLA (AM) :</div> <div>-UNILATERALLY EXAMINED; -PRESENT</div> <div>BONE, FEMUR (FE) :</div> <div>-ARTICULAR SURFACE NOT PRESENT; -PRESENT</div> <div>LACRIMAL GL, EXO (EO) :</div> <div>>UNREMARKABLE</div> <div>LUNG (LU) :</div> <div>-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT</div> <div>-FOREIGN MATERIAL; -PRESENT</div> <div>PARATHYROID (PT) :</div> <div>>SECTION EXAMINED; TISSUE NOT PRESENT</div> </div>

INDIVIDUAL ANIMAL SUMMARY REPORT
STUDY NUMBER: 2399108

ANIMAL NUMBER: B08505
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 04/21/86
STUDY DAY OF DEATH: 11
STUDY WEEK OF DEATH: 2
TERMINAL BODY WEIGHT: 175.2 GRAMS
DATE AND TIME OF NECROPSY: 04/21/86 15:05
PROSECTUR: BARBARA DAY
REORDER: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: NOT REQUIRED BY PROTOCOL
WEIGHER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), AORTA, FEMUR (FF), KIDNEY, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LO), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), AORTA, THORACIC (AO), AORTA, FEMUR (FF), KIDNEY, STERNUM (SR),
CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT),
ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PITUITARY (PI),
RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08506

SEX: FEMALE

DOSE GROUP: 4

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

DATE OF DEATH: 07/14/86

STUDY DAY OF DEATH: 95

STUDY WEEK OF DEATH: 14

TERMINAL BODY WEIGHT: 230.9 GRAMS

DATE AND TIME OF NECROPSY: 07/14/86 14:16

PROSECTOR: BARBARA DAY

RECORDER: SID JONES, DUM, PHD, DACUP

POST-FTX WEIGHT: NOT REQUIRED BY PROTOCOL

PATHOLOGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.058	.0252 %	.0296	WEIGHT TAKEN
OVARY (OV)	.111	.0479 %	.0563	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.96	.851 %	1.000	WEIGHT TAKEN
HEART (HT)	.74	.320 %	.376	WEIGHT TAKEN
SPLEEN (SP)	.54	.233 %	.274	WEIGHT TAKEN
KIDNEY (KD)	1.82	.788 %	.927	WEIGHT TAKEN
LIVER (LT)	8.30	3.595 %	4.276	WEIGHT TAKEN

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGY
-APPEARED NORMAL	<div>STOMACH, NONGL (SU) :</div> <div>-WALL, THICKENED</div> <div>-RAISED AREA; TWO, WHITE, 3 X 3 MM</div> <div>GENERAL INFORMATION (XX) :</div> <div>>NOTE:>EXTERNAL OBSERVATIONS:NONE</div>	<div>ADRENAL, MEDULLA (AM) :</div> <div>-UNILATERALLY EXAMINED,-PRESENT</div> <div>EYE (EY) :</div> <div>-CHRONIC INFLAMMATION, HARDERIAN GLAND,-SLIGHT</div> <div>LUNG (LU) :</div> <div>-PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT</div> <div>STOMACH, MUSE (SU) :</div> <div>-ACANTHOSIS,-MODERATE</div> <div>-INFLAMMATION, CHRONIC,-SLIGHT</div>

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 366

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

ANIMAL NUMBER: B08506
SEX: FEMALE
DATE OF DEATH: 07/14/86
DATE AND TIME OF NECROPSY: 07/14/86 14:16
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL

DOSE GROUP: 4
STUDY WEEK OF DEATH: 14
PROSECTOR: BARBARA DAY
PATHOLOGIST: SID JONES, DVM, PhD, DACVP
SACRIFICE STATUS: SCHEDULED
TERMINAL SACRIFICE
TERMINAL BODY WEIGHT: 230.9 GRAMS
RECORDED: SID JONES, DVM, PhD, DACVP
WEIGHT: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SR),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GI (ST), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), *COLLECTED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), PECTUS (PE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), HEART (HT),
ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GI (ST), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 21991108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08507 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHMIDT, TERMINAL SACRIFICE
 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 258.4 GRAMS
 DATE AND TIME OF NECROPSY: 07/14/86 11:41 PROSECUTOR: DOUGLAS HERMANN RECORDED: SID JONES, DVM, PHD, DATUP
 POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DATUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

^COLLECTED/TAKEN (XN) :
 -ELECTRON MICROSCOPY SAMPLE; LIVER
 GENERAL INFORMATION (XX) :
 >NOTE:EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

BONE, FEMUR (FE) :
 -ARTICULAR SURFACE NOT PRESENT, -PRESENT
 LUNG (LU) :
 -PERIBRONCHIAL/PERIVASCULAR
 INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CC), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
 LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (ON), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
 PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GI (ST), STOMACH, HORS (SH),
 THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE),
 COLON (CO), CORD, CERVICAL (CC), CORD, LUMBAR (LC), CORD, THORACIC (TC), DIAPHRAGM (DI), ESOPHAGUS (ES), EYE (EY),
 HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS),
 MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIUM, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN),
 OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GI (ST),
 STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2392108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808508 SEX: FEMALE DOSE GROUP: 4 SACRIFIC STATUS: SCHEDULED, TERMINAL SACRIFIC
DATE OF DEATH: 07/14/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 233.2 GRAMS
DATE AND TIME OF NECROPSY: 07/14/86 14:26 PROSECTOR: DOUGLAS HERNDEN RECIPIER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE: LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNGS (LUD) : -PULMONARY/PERIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL UTERUS (UT) : -DILATATION,-SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LB), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, BL (ST), STOMACH, MAND (SD),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LB), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, MAND (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2397118

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08509 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 222.0 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 9:45 PROSECUTOR: DRUGLAS HERNDON RECORDED: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XM) :

-ELECTRON MICROSCOPY SAMPLE: LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

JEJUNUM (JE) :

>TISSUE MISSING

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,

INFILTRATION, LYMPHOID, -SLIGHT

PARATHYROID (PT) :

>SECTION EXAMINED; TISSUE NOT PRESENT

UTERUS (UT) :

-DILATATION, -MODERATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), PINE, FEMUR (FE), RIB, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MURSEL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, MURSEL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: B08510 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 211.9 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 11:02 PROSECTOR: BARBARA DAY NECROPSY: SID JONES, DUM, PHO, DAIJUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHO, DAIJUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

UTERUS (UT) :
-LUMEN, FLUID; BOTH HORNS, CLEAR
^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE: LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

LIVER (LI) :
-FOOT OF MODERATE FAT CELLS,-MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID,-SLIGHT
UTERUS (UT) :
-DILATATION,-MODERATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), HBB, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), HBB, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2492188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08511
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86
STUDY DAY OF DEATH: 96
STUDY WEEK OF DEATH: 14
TERMINAL BODY WEIGHT: 242.2 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 12:00
PROSECTOR: DOUGLAS HERNDON
RECIPIENT: SID JONES, DUM, PHD, DADUP
WEIGHTER: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: SID JONES, DUM, PHD, DADUP
WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNG (LJ) : -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LO), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, BL (ST), STOMACH, BONES (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LO), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NERVE, THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

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APPENDIX 8

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 322

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 999188

ANIMAL NUMBER: B08512 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED; TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 265.8 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 9:45 PROSECTOR: BARBARA DAY KETTERER: SID JONES, DUM, PHD, DAIJUP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DAIJUP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

HISTOPATHOLOGY

KIDNEY (KD):
-NEPHROPATHY, CHRONIC PROGRESSIVE,
MINIMAL
LUNG (LU):
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, SLIGHT
MAMMARY GLAND (MG):
-TISSUE MISSING

COLLECTED/TAKEN (XW):
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERVATIONS: NONE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTAL (CS), CORD, LUMBAR (LU), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), SPIFF (SP), STOMACH, IN (SI), STOMACH, NONG (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERUTAL (CS), CORD, LUMBAR (LU), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LIVER (LI),
LN, MESENTERIC (MS), MAND SALIVARY GL (SS), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN),
OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), SKIN (SK), SPIFF (SP), STOMACH, IN (SI),
STOMACH, NONG (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08513 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 236.4 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:04 PROSECUTOR: HARRARA DAY RETURNER: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PhD, DACVP WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-SALIVATION

COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE:>EXTERNAL PRESERVATIONS:SALIVATION

HISTOPATHOLOGY

LIVER (LI) :
-FOOD OF MORPHOLOGY FOR CELLS,-MINIMAL
LUNG (LU) :
-PERIPHERAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-MINIMAL
MAMMARY GLAND (MG) :
>TISSUE MISSING

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (ON), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIFF (SP), STOMACH, ST (ST), STOMACH, MINOR (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARRIUM, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SN),
OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS),
STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

ANIMAL NUMBER: 808514 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 06/20/86 STUDY WEEK OF DEATH: 11 TERMINAL BODY WEIGHT: 251.9 GRAMS
DATE AND TIME OF NECROPSY: 06/20/86 15:38 PROSECTOR: BARBARA DAY REFERRED: BARBARA DAY
POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU) : -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES, LIGHT TO DARK RED GENERAL INFORMATION (XX) : >NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS:NONE	LUNG (LU) : -PERIPHRETIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -SIGHT -FIXATION MATERIAL, -PRESERVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MAND, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGL (SI), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MAND, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGL (SI), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 93991MR

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08515 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: UNSCHEDULED (U)
DATE OF DEATH: 04/20/86 STUDY WEEK OF DEATH: 2 TERMINAL BODY WEIGHT: 128.8 GRAMS
DATE AND TIME OF NECROPSY: 04/20/86 12:00 PROSECUTOR: KIM LINCOLN
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

LUNG (LU) :

-FAILURE TO COLLAPSE; ALL LUNGES, FLUID FILLED

-NOTIFIED: ALL LUNGES

GENERAL INFORMATION (XX) :

(NOTE) LAST IN-LIFE AND EXTERNAL OBSERVATIONS: ANIMAL WENT INTO A FULL CONVULSION AND DIED SEVERAL MINUTES AFTER SAVAGE DISSECTION

HISTOPATHOLOGY

LUNG (LU) :

-FOREIGN MATERIAL: -PRESENT

-EDEMA: -MODERATE

MAMMARY GLAND (MG) :

>TISSUE MISSING

PARATHYROID (PT) :

>SECTION EXAMINED; TISSUE NOT PRESENT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JJ), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, BL (SL), STOMACH, NING (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ~COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JJ), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2397186

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08516 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 265.2 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 14:14 PROSECTOR: DOUGLAS HERNDON REORDER: SID JONES, DVM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DVM, PHD, DACUP WETTER: DOUGLAS HERNDON

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.076	.0286 %	.0369	WEIGHT TAKEN
OVARY (OU)	.125	.0473 %	.0611	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.05	.775 %	1.000	WEIGHT TAKEN
HEART (HT)	.92	.347 %	.449	WEIGHT TAKEN
SPLEEN (SP)	.61	.230 %	.297	WEIGHT TAKEN
KIDNEY (KO)	2.11	.796 %	1.028	WEIGHT TAKEN
LIVER (LI)	9.01	3.397 %	4.386	WEIGHT TAKEN

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS

CECUM (CE) :
-DARK AREA; IN WALL, ONE, DARK RED;
1.0 X 0.5 CM
>NOTE: >DARK AREA, POSSIBLE INJECTION SITE
UTERUS (UT) :
-LUMEN, FLUID; BOTH HORNS, CLEAR
GENERAL INFORMATION (XX) :
>NOTE: >EXTERNAL OBSERVATIONS: NONE

HISTOPATHOLOGY

CECUM (CE) :
-SUBMUCOSA F
LIVER (LI) :
-FOCI OF MONONUCLEAR CELLS, -MINIMAL
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -MINIMAL
UTERUS (UT) :
-DILATATION, -MODERATELY SEVERE

APPENDIX B
 *** PATH/TOX SYSTEM OUTPUT ***
 SUBCHRONIC TOXICITY STUDY IN RATS

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 PAGE: 377

STUDY NUMBER: 2399108

HAZLETON LABORATORIES AMERICA, INC.
 DEPARTMENT OF PATHOLOGY

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808516 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCEDDIED. TERMINAL SACRIFICE
 DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 265.2 GRAMS
 DATE AND TIME OF NECROPSY: 07/15/86 14:14 PROSECTOR: DOUGLAS HERNDON RETAINER: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHTER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: DOUGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), RIB, STERNUM (SR),
 BRAIN W/STEM (BR), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU),
 ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI),
 LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
 MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
 SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY),
 TRACHEA (TR), URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), RIB, STERNUM (SR),
 BRAIN W/STEM (BR), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU),
 ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
 LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
 NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
 SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 378

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2397108

ANIMAL NUMBER: B08517 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 223.0 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 14:51 PROSECTOR: BARBARA DAY RECORDER: SID JONES, DUM, PHD, DACUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHTER: BARBARA DAY

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN	
				ST	ATUS
ADRENAL (AD)	.077	.0345 %	.0372	WEIGHT	TAKEN
OVARY (OV)	.117	.0525 %	.0565	WEIGHT	TAKEN
BRAIN W/STEM (BR)	2.07	.928 %	1.000	WEIGHT	TAKEN
HEART (HT)	.70	.314 %	.338	WEIGHT	TAKEN
SPLEEN (SP)	.48	.215 %	.232	WEIGHT	TAKEN
KIDNEY (KD)	1.96	.879 %	.947	WEIGHT	TAKEN
LIVER (LI)	8.25	3.700 %	3.986	WEIGHT	TAKEN

PATHOLOGY OBSERVATIONS

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LU) :

-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

HISTOPATHOLOGY

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08517 SEX: FEMALE DOSE GROUP: 4 SACRIFICIAL STATUS: SCHMIDT, TERMINAL SACRIFICIAL
 DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 223.0 GRAMS
 DATE AND TIME OF NECROPSY: 07/15/86 14:51 PRESECTOR: BARBARA DAY AFTERDEATH: SID JONES, DUM, PHD, DAIUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DAIUP WEIGHT: BARBARA DAY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
 LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
 MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SC), PANCREAS (PA), PARATHYROID (PT),
 PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SO), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN),
 THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), VULVA/VAGINA (VU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),
 BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
 DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
 LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
 NERVE, SCIATIC (SC), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
 SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
 UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08518
 SEX: FEMALE
 DOSE GROUP: 4
 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
 DATE OF DEATH: 07/16/86
 STUDY DAY OF DEATH: 97
 STUDY WEEK OF DEATH: 14
 TERMINAL BODY WEIGHT: 239.8 GRAMS
 DATE AND TIME OF NECROPSY: 07/16/86 10:30
 PROSECTOR: TIM GROVE
 RECORDER: SID JONES, DUM, PHD, DACUP
 POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL
 PATHOLOGIST: SID JONES, DUM, PHD, DACUP
 WEIGHTER: TIM GROVE

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN S T A T I S
ADRENAL (AD)	.068	.0284 %	.0362	WEIGHT TAKEN
OVARY (OV)	.115	.0480 %	.0612	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.88	.784 %	1.0000	WEIGHT TAKEN
HEART (HT)	.77	.321 %	.410	WEIGHT TAKEN
SPLEEN (SP)	.53	.221 %	.282	WEIGHT TAKEN
KIDNEY (KD)	1.88	.784 %	1.0000	WEIGHT TAKEN
LIVER (LI)	7.73	3.224 %	4.112	WEIGHT TAKEN

PATHOLOGY OBSERVATIONS

NECROPSY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

LUNG (LID) :

-PERITONEAL/PERICARDIAR, INFILTRATION, LYMPHOID, -SLIGHT

HISTOPATHOLOGY

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 381

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08518 SEX: FEMALE DISE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 239.8 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:30 PROSECTOR: TIM GROVE PATHOLOGIST: SID JONES, DVM, PhD, DACVP REFERRER: SID JONES, DVM, PhD, DACVP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL WEIGHTER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ACQUIESCED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 382

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08519 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 284.1 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 11:55 PROSECTOR: DOUGLAS HERNDON RECORDED: SID JONES, DUM, PHD, DATUP
POST-FIX METHOD: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DATUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

HISTOPATHOLOGY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

^COLLECTED/TAKEN (XU) :

-ELECTRON MICROSCOPY SAMPLE: LIVER

GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE

LIVER (LU) :

-FOCI OF MONONUCLEAR CELLS, -SI TNIT

LUNG (LU) :

-PERIPHONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID, -SI TNIT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK), NERVE, SCIATIC (SI), OVARY (OV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GI (ST), STOMACH, NONGL (SN),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SK),
NERVE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB),
UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

INDIVIDUAL ANIMAL SUMMARY REPORT
STUDY NUMBER: 2309108

ANIMAL NUMBER: B08520
SEX: FEMALE
DOSE GROUP: 4
SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 05/29/86
STUDY WEEK (IF DEATH: 7
TERMINAL BODY WEIGHT: 214.2 GRAMS
DATE AND TIME OF NECROPSY: 05/29/86 11:05
PROSECTOR: BARBARA DAY
RECORDED BY: BARBARA DAY
POST-FIX METHOD: NOT REQUIRED BY PROTOCOL
PATHOLOGIST: NOT REQUIRED BY PROTOCOL
WEIGHTER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S		HISTOPATHOLOGY
CLINICAL OBSERVATIONS	NECROPSY	
-APPEARED NORMAL	LUNG (LU) : -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES, LIGHT TO DARK RED GENERAL INFORMATION (XX) : >NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS: DARK RED FLUID SURROUNDING NARES	CECUM (CE) : >AUTOLYTIC COLON (CO) : >AUTOLYTIC DUODENUM (DU) : >AUTOLYTIC ILEUM (IL) : >AUTOLYTIC JEJUNUM (JE) : >AUTOLYTIC LUNG (LU) : -FOREIGN MATERIAL, -PRESENT -EDEMA, -MODERATE RECTUM (RE) : >AUTOLYTIC

APPENDIX B

HAZLETON LABORATORIES AMERICA, INC.
DEPARTMENT OF PATHOLOGY

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 384

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2199108

ANIMAL NUMBER: B08520 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: UNSCHEDULED (D)
DATE OF DEATH: 05/29/86 STUDY DAY OF DEATH: 49 STUDY WEEK OF DEATH: 7 TERMINAL BODY WEIGHT: 214.2 GRAMS
DATE AND TIME OF NECROPSY: 05/29/86 11:05 PROSECTOR: BARBARA DAY REORDER: BARBARA DAY
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHT: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILLUM (IL), ILLUM (IF), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LO), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRUM, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SI), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), UNCOLLECTED/TAKEN (XU)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), ESOPHAGUS (ES), EYE (EY), HEART (HT),
KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARRUM, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SI), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88
PAGE: 385

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2492188

ANIMAL NUMBER: B08521 SEX: FEMALE DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 258.6 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 12:28 PROSECTOR: DOUGLAS HERNDON REFERENCE: SID JONES, DUM, PHO, DAIJUP
POST-FIX WEIGHT: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHO, DAIJUP WEIGHT: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

P A T H O L O G Y O B S E R V A T I O N S

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

LN, MESENTERIC (MS) :
-DARK AREA; ONE, DARK RED, 7 X 4 MM
>NOTE>DARK AREA, POSSIBLE INJECTION SITE

^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE>EXTERNAL OBSERVATIONS:NONE

HISTOPATHOLOGY

EYE (EY) :
-CHRONIC INFLAMMATION; HADLERIAN GLAND,
SLIGHT
LN, MESENTERIC (MS) :
-CONGESTION, SLIGHT
LUNG (LU) :
-PERIBRONCHIAL/PERIVASCULAR
INFILTRATION, LYMPHOID, SLIGHT

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CEREBRAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, OTHER (LO), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIUM, STERNUM (SP),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, BL (ST), STOMACH, NITRAI (SD), THYRUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CEREBRAL (CS), CORD, LUMBAR (LD), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI),
MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIUM, STERNUM (SP), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN),
OVARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (SD),
STOMACH, NITRAI (SD), THYRUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***



HAZLETON

LABORATORIES AMERICA, INC.

1330 - B PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

HLA 2399-108

- 386 -

APPENDIX 9

Analytical Chemistry Report



HAZLETON

LABORATORIES AMERICA, INC.

1330 - B PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

SPONSOR: DYNAMAC CORPORATION

MATERIAL: M-XYLENE (M-XYLOL) CAS 108-38-3

SUBJECT: FINAL REPORT
Subchronic Toxicity Study
m-Xylene in Corn Oil Gavage Formulations
Project No. 2399-108

1. OBJECTIVE:

The purpose of this study was to perform chemical analyses of corn oil gavage formulations to determine dose concentrations of m-xylene in preparations used for toxicological testing in rats.

2. MATERIAL:

The m-xylene used in this study, Lot #259211, Batch 286, was obtained from Fluka Chemical Corporation, Hauppauge, New York. It was received March 6, 1986 and assigned LH No. 10,031A. The manufacturer's stated purity was 99%.

3. METHOD AND PROCEDURES

A. Method

The method for the determination of m-xylene in corn oil gavage preparations was developed by Hazleton Biotechnologies Company. In brief, m-xylene is extracted from the corn oil by shaking with methanol. Following centrifugation, appropriate dilutions are made of the extracts, incorporating n-propylbenzene as the internal standard. The extracts are analyzed by gas chromatography (GC) using a flame ionization detector. Matrix standard solutions carried through the procedure are used for the standard curve and instrument calibration. The complete method is included in this report in Attachment A.

Analysis of corn oil for peroxides was performed using the Official Method Cd. 8-53 of the A.O.C.S. (1972). It determines all substances, in terms of milliequivalents (meq) of peroxide per 1000 grams of sample, which oxidize aqueous iodide under the conditions of the test.



3. METHOD AND PROCEDURES (Continued)

B. Procedures

The chemical characterization of the test material was performed prior to the study start. Identity was determined using infrared (IR), nuclear magnetic resonance (NMR) and mass spectrometry (MS) spectral techniques. Elemental analysis and the determination of water using the Karl Fischer technique were also carried out. A gas chromatographic (GC) scan was run to assess the purity of the chemical.

Upon receipt of the test material, aliquots were taken and stored at -20°C for use as reference standards for subsequent reanalysis. At the end of the study, GC scans for purity were performed on the bulk chemical and the reference standard to assess the integrity of the test chemical under the storage conditions during the study.

The initial method validation for dose verification analysis was performed on matrix standards at 4 levels of concentration (excluding 0). Four standards were prepared at the high and low levels and a single standard at each midpoint. Linear regression analysis was carried out on the results of the standard curve.

In addition, analyses of gavage preparations at the high and low levels of concentration were carried out on two different days to show linearity, precision, accuracy, and reproducibility of the method.

Stability of m-xylene in the corn oil gavage preparations at the high and low dosage concentrations was determined after 7, 14, and 21 days of storage at room temperature and at 5°C .

Dose verification analyses of the corn oil gavage formulations were performed at Weeks 1, 5, 9, and 13 of the study.

Each batch of corn oil used for the preparation of gavage dosing formulations was analyzed for peroxides prior to its first use and at monthly intervals thereafter.

4. RESULTS AND CONCLUSIONS

The purity and identity data for the chemical characterization of the test material are presented in this report as Attachment B.

Tables 1 and 2 contain the analytical method validation data for the determination of m-xylene in corn oil gavage formulations. The RSDs for the four analyses at the high and low points on the standard curve, $\pm 0.25\%$ and



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4. RESULTS AND CONCLUSION (Continued)

+ 0.96, respectively, show excellent precision. The correlation coefficients presented in both tables demonstrate linearity within the range of 0.20 to 1.0 ug m-xylene injected.

Analyses of the gavage samples at the high and low dose concentrations on different days show good method reproducibility and accuracy.

Stability data for m-xylene in corn oil gavage formulations at 40.40 and 323.2 mg/mL concentrations stored at 5°C and room temperature are presented in Tables 3 and 4. After 21 days there was a mean percent loss of 2.8 for samples stored at 5°C and 1.7 for those stored at room temperature. These data clearly indicate the required stability of m-xylene in corn oil for this study.

Results of the dose verification analyses of the gavage preparations for m-xylene can be found in Table 5. All of the samples analyzed were within the acceptable + 10% of target concentration. Eight samples had < 1.0% agreement between duplicate analyses. The duplicate analyses of 3 samples agreed within 2.5% and the duplicates of one sample varied by 4.3%.

Table 6 presents a summary of the analyses performed to determine peroxides in corn oil. For this study, corn oil with a peroxide number equal to or greater than 10 meq/kg was considered rancid and not acceptable for use. The peroxide number for each analysis was well below the acceptable limit. Copies of the individual reports are included to provide detailed information about the corn oil used and the cumulative results of testing.

Reported by:

Lee Hohing
Research Associate

Date

Approved by:

Susan A. Lewis, Ph.D.
Staff Scientist



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PROJECT NO. 2399-108

TABLE 1

ANALYTICAL METHOD VALIDATION DATA FOR M-XYLENE MATRIX STANDARD PREPARATIONS

M-XYLENE INJECTED (ug)	M-XYLENE FOUND (FROM THE CALIBRATION STANDARD CURVE) (ug)
1.00	0.999 \bar{x} = 0.999 1.002 SD = + 0.0025 0.996 RSD = \pm 0.25% 1.000
0.80	0.800
0.40	0.403
0.20	0.199 \bar{x} = 0.198 0.195 SD = + 0.0019 0.198 RSD = \pm 0.96% 0.199

Linear Regression Analysis Using Area Ratio:

Correlation coefficient: 1.0000
Intercept : 0.0003
Slope : 0.8989



PROJECT NO. 2399-108

TABLE 2

ANALYTICAL METHOD VALIDATION DATA FOR THE DETERMINATION
OF M-XYLENE IN CORN OIL GAVAGE PREPARATIONS

SAMPLE IDENTIFICATION	TARGET VALUE (mg/mL)	DATE ANALYZED	ASSAY VALUE (mg/mL)	PERCENT OF TARGET
Control	0.00	4/03/86	N.D.	N/A
R0-0277-86A	40.40	4/03/86	38.80	96.04
R0-0277-86B	40.40	4/03/86	39.20	97.03
R0-0278-86A	323.2	4/03/86	315.0	97.46
R0-0278-86B	323.2	4/03/86	313.5	97.00
Control	0.00	4/04/86	N.D.	N/A
R0-0277-86A	40.40	4/04/86	38.90	96.29
R0-0277-86B	40.40	4/04/86	38.65	95.67
R0-0278-86A	323.2	4/04/86	310.5	96.07
R0-0278-86B	323.2	4/04/86	310.5	96.07

STANDARD CURVE STATISTICAL ANALYSIS

Date of Analysis (date extracted):	4/03/86	4/04/86
Correlation Coefficient	: 0.9999	1.0000
Intercept	: 0.0013	(-)0.0009
Slope	: 0.8968	0.9057

N.D. = None Detected
N/A = Not Applicable


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PROJECT NO. 2399-108

TABLE 3

STABILITY OF M-XYLENE IN CORN OIL GAVAGE FORMULATIONS STORED AT 5°C

SAMPLE IDENTIFICATION	DATE FORMULATED	DATE ANALYZED	STORAGE PERIOD	TARGET VALUE (mg/mL)	ASSAY VALUE (mg/mL)	PERCENT OF ORIGINAL \bar{x} VALUE
R0-0277-86A R0-0277-86B	4/03/86	4/03/86	None	40.40 40.40	38.80 39.20 $\bar{x} = 39.00$	N/A N/A
R0-0278-86A R0-0278-86B	4/03/86	4/03/86	None	323.2 323.2	315.0 313.5 $\bar{x} = 314.3$	N/A N/A
R0-0277-86A R0-0277-86B	4/03/86	4/10/86	7 Days	40.40 40.40	39.75 39.55	102 101
R0-0278-86A R0-0278-86B	4/03/86	4/10/86	7 Days	323.2 323.2	324.5 324.0	103 103
R0-0277-86A R0-0277-86B	4/03/86	4/17/86	14 Days	40.40 40.40	39.20 39.15	101 100
R0-0278-86A R0-0278-86B	4/03/86	4/17/86	14 Days	323.2 323.2	312.5 312.0	99.4 99.3
R0-0277-86A R0-0277-86B	4/03/86	4/24/86	21 Days	40.40 40.40	39.30 39.30	101 101
R0-0278-86A R0-0278-86B	4/03/86	4/24/86	21 Days	323.2 323.2	302 309	96.1 98.3

N/A = Not Applicable

L:50/3-3



PROJECT NO. 2399-108

TABLE 4

STABILITY OF M-XYLENE IN CORN OIL GAVAGE FORMULATIONS STORED AT ROOM TEMPERATURE

SAMPLE IDENTIFICATION	DATE FORMULATED	DATE ANALYZED	STORAGE PERIOD	TARGET VALUE (mg/mL)	ASSAY VALUE (mg/mL)	PERCENT OF ORIGINAL \bar{x} VALUE
R0-0277-86A R0-0277-86B	4/03/86	4/03/86	None	40.40 40.40	38.80 39.20 $\bar{x} = 39.00$	N/A N/A
R0-0278-86A R0-0278-86B	4/03/86	4/03/86	None	323.2 323.2	315.0 313.5 $\bar{x} = 314.3$	N/A N/A
R0-0277-86A R0-0277-86B	4/03/86	4/10/86	7 Days	40.40 40.40	39.60 39.50	102 101
R0-0278-86A R0-0278-86B	4/03/86	4/10/86	7 Days	323.2 323.2	318.0 317.0	101 101
R0-0277-86A R0-0277-86B	4/03/86	4/17/86	14 Days	40.40 40.40	39.30 39.35	101 101
R0-0278-86A R0-0278-86B	4/03/86	4/17/86	14 Days	323.2 323.2	314.0 312.5	99.9 99.4
R0-0277-86A R0-0277-86B	4/03/86	4/24/86	21 Days	40.40 40.40	39.40 39.40	101 101
R0-0278-86A R0-0278-86B	4/03/86	4/24/86	21 Days	323.2 323.2	309.0 309.0	98.3 98.3

N/A = Not Applicable



PROJECT NO. 2399-108

TABLE 5

DETERMINATION OF M-XYLENE IN CORN OIL
GAVAGE PREPARATIONS TO VERIFY DOSAGE CONCENTRATION

SAMPLE IDENTIFICATION	DATE FORMULATED	DATE ANALYZED	INTERVAL	TARGET VALUE (mg/mL)	ASSAY VALUE (mg/mL)	PERCENT OF TARGET
R0-0295-86	4-09-86	4-09-86	Week 1	0.00	N.D.	N/A
R0-0296-86A	4-09-86	4-09-86	"	40.40	38.70	95.79
R0-0296-86B	4-09-86	4-09-86	"	40.40	38.90	96.29
R0-0297-86A	4-09-86	4-09-86	"	80.80	78.90	97.65
R0-0297-86B	4-09-86	4-09-86	"	80.80	78.50	97.15
R0-0298-86A	4-09-86	4-09-86	"	323.2	323.5	100.00
R0-0298-86B	4-09-86	4-09-86	"	323.2	322.5	99.78
R0-0404-86	5-07-86	5-12-86	Week 5	0.00	N.D.	N/A
R0-0405-86A	5-07-86	5-12-86	"	40.40	39.10	96.78
R0-0405-86B	5-07-86	5-12-86	"	40.40	39.10	96.78
R0-0406-86A	5-07-86	5-12-86	"	80.80	78.70	97.40
R0-0406-86B	5-07-86	5-12-86	"	80.80	78.80	97.52
R0-0407-86A	5-07-86	5-12-86	"	323.2	317.0	98.08
R0-0407-86B	5-07-86	5-12-86	"	323.2	314.5	97.31
R0-0520-86	6-03-86	6-06-86	Week 9	0.00	N.D.	N/A
R0-0521-86A	6-03-86	6-06-86	"	40.40	36.45	90.22
R0-0521-86B	6-03-86	6-06-86	"	40.40	38.20	94.55
R0-0522-86A	6-03-86	6-06-86	"	80.80	78.10	96.66
R0-0522-86B	6-03-86	6-06-86	"	80.80	76.20	94.31
R0-0523-86A	6-03-86	6-06-86	"	323.2	315.0	97.46
R0-0523-86B	6-03-86	6-06-86	"	323.2	307.5	95.14
R0-0708-86	7-01-86	7-03-86	Week 13	0.00	N.D.	N/A
R0-0709-86A	7-01-86	7-03-86	"	40.40	38.95	96.41
R0-0709-86B	7-01-86	7-03-86	"	40.40	38.10	94.31
R0-0710-86A	7-01-86	7-03-86	"	80.80	78.10	96.66
R0-0710-86B	7-01-86	7-03-86	"	80.80	78.60	97.28
R0-0711-86A	7-01-86	7-03-86	"	323.2	313.5	97.00
R0-0711-86B	7-01-86	7-03-86	"	323.2	316.5	97.93

N.D. = None Detected
N/A = Not Applicable



PROJECT NO. 2399-108

TABLE 6

ANALYSES OF CORN OIL FOR PEROXIDE DETERMINATION

<u>SAMPLE IDENTIFICATION</u>	<u>DATE OF ANALYSIS</u>	<u>PEROXIDE NUMBER FROM EACH INDIVIDUAL TITRATION (meq/kg)</u>
RO-0318-86	04-21-86	1.11 1.07 1.04 $\bar{x} = \frac{1.07}{\underline{\quad}} \pm 0.035 \text{ S.D.}$
RO-0454-86	05-19-86	1.14 1.14 1.13 $\bar{x} = \frac{1.13}{\underline{\quad}} \pm 0.006 \text{ S.D.}$
RO-0588-86	06-20-86	1.37 1.37 1.37 $\bar{x} = \frac{1.37}{\underline{\quad}} \pm 0.000 \text{ S.D.}$
RO-0810-86	07-17-86	1.63 1.64 1.63 $\bar{x} = \frac{1.63}{\underline{\quad}} \pm 0.006 \text{ S.D.}$



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ATTACHMENT A

1. Determination of m-Xylene in Corn Oil Gavage
(Analytical Method No. 165)
2. Analysis of Corn Oil for Peroxides; Modification of the
Official Method of the American Oil Chemists' Society



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DIAGNOSTIC ASSAYS DEPARTMENT
ANALYTICAL CHEMISTRY LABORATORY

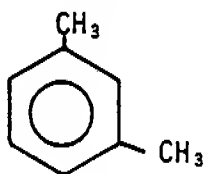
ANALYTICAL METHOD NO. 165

PAGE 1 OF 7

DATE: March 24, 1986
APPROVED: *Susan A. Hewes*

TITLE: Determination of M-Xylene in Corn Oil Gavage

STRUCTURE:



Meta-xylene

DEVELOPED BY: Hazleton Biotechnologies Company, a Division of Hazleton Laboratories Corporation

1.0 SCOPE

This method is for the gas chromatographic (GC) analysis of m-xylene in corn oil gavage at levels from 40 mg/mL to 320 mg/mL.

2.0 PRINCIPLE

m-Xylene is extracted from the corn oil by shaking with methanol. The extracts are analyzed by gas chromatography (GC) using a flame ionization detector (FID).

3.0 EQUIPMENT

- 3.1 Gas Chromatograph: Hewlett-Packard 5880A equipped with a flame ionization detector (FID), a HP 5880A terminal and a HP 7672A autosampler, or equivalent
- 3.2 Glass Column: 6 ft x 2 mm packed with GP 5% SP-1200/1.75% Bentone 3H on 100/120 Supelcoport, or equivalent
- 3.3 Polypropylene Tubes: Falcon 2070 blue max 50 mL
- 3.4 Analytical Balance: Mettler H31AR, or equivalent
- 3.5 Shaker Box: Equipoise heavy duty, or equivalent
- 3.6 SMI Pipet: 0.1 mL x 0.5 mL SMI pipets, or equivalent
- 3.7 Centrifuge: International centrifuge, model K or equivalent
- 3.8 General Laboratory Glassware

4.0 REAGENTS

- 4.1 Methanol: Baker "HPLC grade", or equivalent
- 4.2 m-Xylene Standard: Fluka Chemical Corp., Cat. No. 95672. Stored at 5°C.
- 4.3 n-Propylbenzene Internal Standard: Supplied by Kodak, Cat. No. 1132224, Lot No. A13B, stored at 5°C

5.0 PROCEDURE

5.1 Standard Preparation

5.1.1 Preparation of Stock standard solutions

Stock Standard Solution I (10.0 mg/mL): Weigh accurately 500 mg of standard m-xylene (adjust for purity) into a 50 mL volumetric flask. Dissolve and bring to volume with methanol.

Stock Standard Solution II (20.0 mg/mL): Weigh accurately 1000 mg of standard m-xylene (adjust for purity) into a 50 mL volumetric flask. Dissolve and bring to volume with methanol.

5.1.2 Preparation of stock internal standard

Weigh accurately 250 mg of the internal standard n-propylbenzene into a 50 mL volumetric flask. Dissolve and bring to volume with methanol. This internal standard contains 5 mg/mL of propylbenzene.

5.1.3 Preparation of Working Matrix Standard Solutions

Prepare the working matrix standard solutions in 50 mL polypropylene tubes as follows:

<u>Std. Soln. No.</u>	<u>mL Undosed Corn Oil</u>	<u>mL Stock Std. I</u>	<u>mL Stock Std. II</u>	<u>mL Methanol</u>	<u>Conc. of Extract mg/mL</u>
1	0.5	1	-	9	1.0
2	0.5	-	1	9	2.0
3	0.5	-	2	8	4.0
4	0.5	5	-	5	5.0

Shake polypropylene tubes on floor shaker for 5 minutes.

Centrifuge at 2500 rpm for 5 minutes.

Dilute extract as follows:

Std. Soln. No.	mL Extract	mL Stock Internal Std.	mL Methanol	Final Concentration (mg/mL) m-xylene	I STD
1	1	1	8	0.1	0.5
2	1	1	8	0.2	0.5
3	1	1	8	0.4	0.5
4	1	1	8	0.5	0.5

Inject 2 μ L of each working matrix standard for standard curve and calibrate.

5.2 Sample Preparation

5.2.1 Pipet 0.5 mL of sample into 50 mL polypropylene tubes.

5.2.2 Pipet 10 mL methanol into each sample tube.

5.2.3 Shake sample tubes on floor shaker for 5 minutes.

5.2.4 Centrifuge at 2500 rpm for 5 minutes.

5.2.5 Make dilutions of the extracts with methanol in 10 mL volumetric flask as follows:

Level	mL Extract	mL Internal Std.	Final Conc. (mg/mL) m-xylene	ISTD
Control	2	1	0.1	0.5
40 mg/mL	2	1	0.2	0.5
80 mg/mL	1	1	0.4	0.5
320 mg/mL	0.2	1	0.5	0.5

5.2.6 Bring to 10 mL volume mark with methanol.

5.2.7 Inject 2 μ L of sample on GC-FID.

5.2.8 Extracts should be refrigerated if not analyzed on the same day.

5.3 Sample Calculation

5.3.1 The Hewlett-Packard GC terminal is programmed to calculate the amount of m-xylene injected from peak area using internal standard procedure for calculating the chromatographic data. The calibration table is generated by analyzing the chromatographic standards listed in 5.1.3.

5.3.2

$$\text{mg detected} = \frac{\text{ug detected}}{\text{mL sample injected}}$$

$$\text{percent target} = \frac{\text{mg detected}}{\text{target}} \times 100$$

$$\text{where mL sample inj.} = \text{inj. vol.} \times \frac{\text{mL sample}}{\text{extraction volume}} \times \frac{\text{aliquot taken for dil.}}{\text{final dil. vol.}}$$

7.0 INSTRUMENT PARAMETERS

Gas Chromatograph : Hewlett-Packard 5880A with flame ionization detector, a HP 5880A terminal, and a HP 7672A autosampler, or equivalent

Column : 6 ft x 2 mm glass column packed with GP 5% SP-1200/1.75% Bentone 34 on 100/120 Supelcoport, or equivalent

Gas Flow

Carrier Gas : Helium, ~ 30 mL/min

Detector Gas : Air, ~ 60 mL/min

Hydrogen, ~ 30 mL/min

Temperature

Oven : 75°C

Detector : 280°C

Injection Port : 150°C

Injection Volume : 2 uL

Chart Speed : 0.25 cm/min

Quantitation : Peak Area Ratio

Retention Time : Approx. 4.9 minutes for m-xylene; ~ 8 minutes for ISTD

NOTE: The above conditions may be changed to optimize the instrument response and sample detection.

ANALYTICAL METHOD NO. 165

PAGE 7 OF 7

DATE: March 24, 1986

8.0 LIST OF FIGURES

Figure 1. Typical chromatograms, standards

Figure 2. Typical standard curve

Figure 3. Typical chromatograms, samples

FIG 1 : TYPICAL CHROMATOGRAMS, STANDARDS

LIST ATTN 2+
ATTN = 215

LIST AUTO SEQ 5
LIST INJ 1 TEMP
INJ 1 TEMP=150°C SETPT=150°C LIMIT=405°C

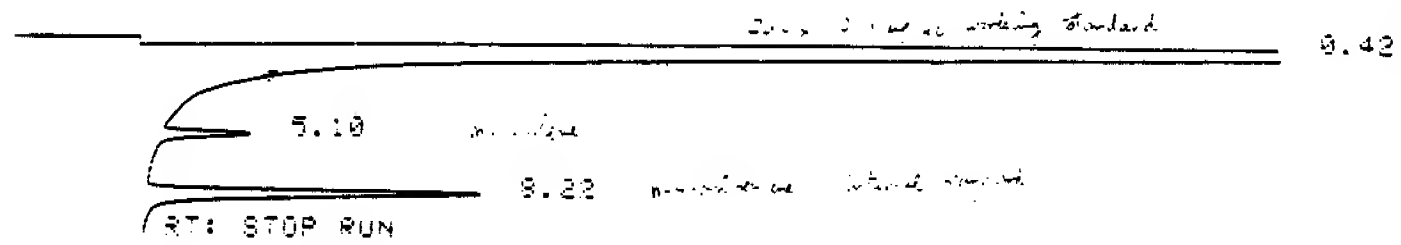
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LIST OVEN TEMP
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EDIT AUTO SEQ 6: 1

EDIT AUTO SEQ 7: 1

START AUTO SEQ



*** 3880A SAMPLER INJECTION @ 17:43 APR 17, 1986
SAMPLE # : ID CODE :

METHOD ABORTED
AREA %

RT	AREA	TYPE	WIDTH	HEIGHT	BASLINE	AREA %
0.00						
0.00						
0.00						
0.42	910859.00	SV	0.07	207103.00	7.94	99.523
5.10	647.60	SB	0.292	35.94	16.76	0.071
8.22	3720.89	SB	0.427	136.33	11.26	0.407

TOTAL AREA = 915227.00
MULTIPLIER = 1

CALIB 1
CALIB AREA OR HEIGHT (1=HEIGHT) 0

REF	RT	AMT	REF	NAME
1	0.420	:		
1	5.099	: .2	:	: M-XYLENE
2	8.223	: 1.0	: +1070	: PROPYLBENZEN

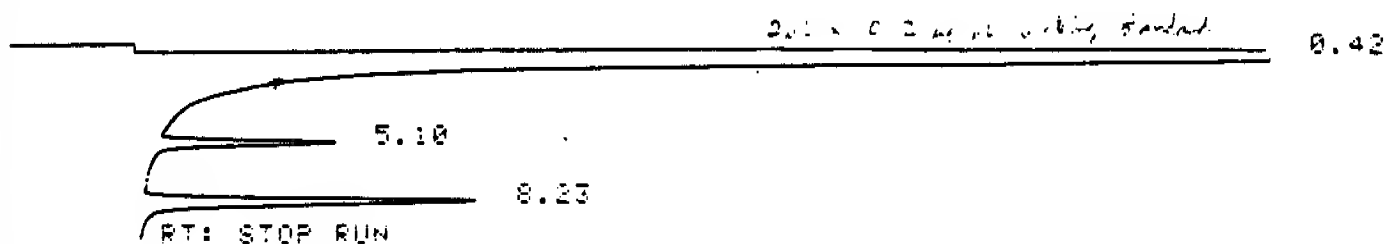
0 MULTIPLIER = 1 :
-1 REF WINDOW = 5% :
-2 NON-REF WINDOW = 5% :
-3 UNCAL REF = 0 :
-4 READING

PROJ. 2389-113 DAY 14 STAB AT RT: 5.100
PROJ. 2389-108 DAY 14 STAB AT RT: 5.090

EDIT AUTO SEQ 6: 2

EDIT AUTO SEQ 7: 2

START AUTO SEQ



[AP] 5880A SAMPLER INJECTION @ 17:58 APR 17, 1986

SAMPLE # : ID CODE :

2

PROC. 2399-108 DAY 14 STAB AT RT & SDEG

1STD

RT	EXP RT	AREA	TYPE	WIDTH	CAL	AMOUNT	NAME
0.00							
0.00							
0.00							
5.10	5.11	1329.17	BB	0.286	1	0.408	M-XYLENE
8.23	8.23	3746.16 +	BB	0.429	2	1STD 1	PROPYLBENZEN

MULTIPLIER = 1

1STD 1 AMT = 1

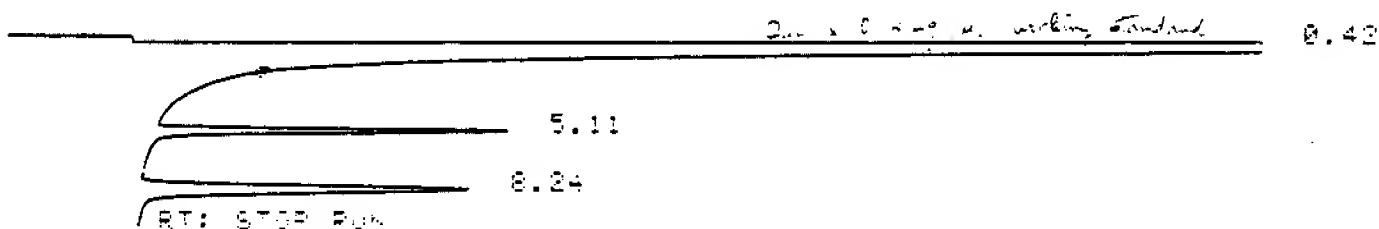
CALIB 2

CAL	RT	NAME	AMT
1	5.105	M-XYLENE	: .4
2	8.234	PROPYLBENZEN	: 1.0

EDIT AUTO SEQ 6: 3

EDIT AUTO SEQ 7: 3

START AUTO SEQ



[AP] 5880A SAMPLER INJECTION @ 18:14 APR 17, 1986

SAMPLE # : ID CODE :

3

PROC. 2399-108 DAY 14 STAB AT RT & SDEG

1STD

RT	EXP RT	AREA	TYPE	WIDTH	CAL	AMOUNT	NAME
0.00							
0.00							
0.00							
5.11	5.11	1329.17	BB	0.286	1	0.408	M-XYLENE
8.24	8.24	3746.16 +	BB	0.429	2	1STD 1	PROPYLBENZEN

MULTIPLIER = 1
ISTD 1 AMT = 1

FIG 1: TYPICAL CHROMATOGRAMS, STANDARDS

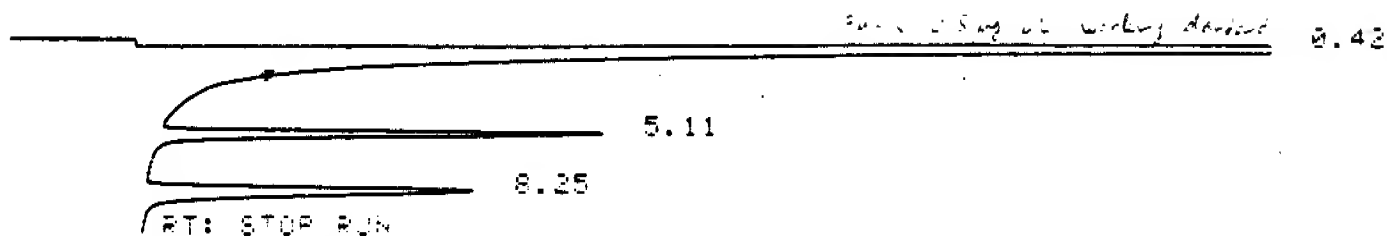
CALIB 3

CAL	RT	NAME	AMT
1	5.110	M-XYLENE	: .8
2	8.241	PROPYLBENZEN	: 1.0

EDIT AUTO SEQ 6: 4

EDIT AUTO SEQ 7: 4

START AUTO SEQ



[-P] 5880A SAMPLER INJECTION @ 18:29 APR 17, 1986

SAMPLE #: ID CODE :

4

PROD. 2399-108 DAY 14 STAB AT RT & SDEG

ISTD

RT	EXP RT	AREA	TYPE	WIDTH	CAL	AMOUNT	NAME
0.00		BASELINE @ START RUN = 7.14					
0.00		THRESHOLD @ START RUN = 4					
0.00		PEAK WIDTH @ START RUN = 0.08					
5.11	5.11	3322.48	BB	0.286	1	1.004	M-XYLENE
8.25	8.25	3702.75 +	BB	0.429	2	ISTD 1	PROPYLBENZEN

MULTIPLIER = 1

ISTD 1 AMT = 1

CALIB B 1

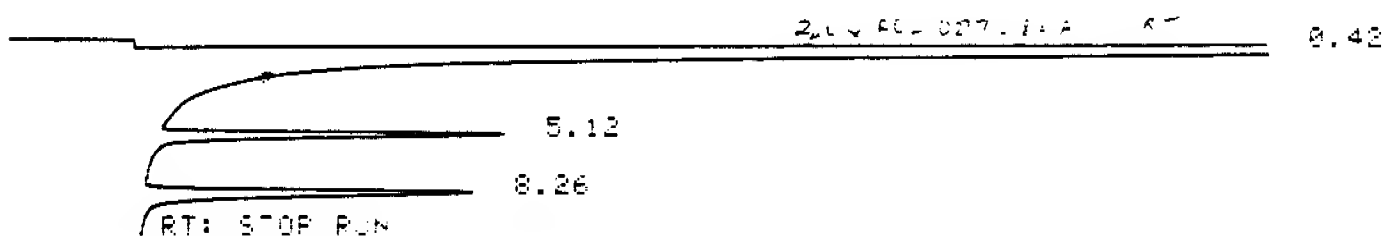
CALIB 4

CAL	RT	NAME	AMT
1	5.112	M-XYLENE	: 1.0
2	8.247	PROPYLBENZEN	: 1.0

EDIT AUTO SEQ 6: 5

EDIT AUTO SEQ 7: 13

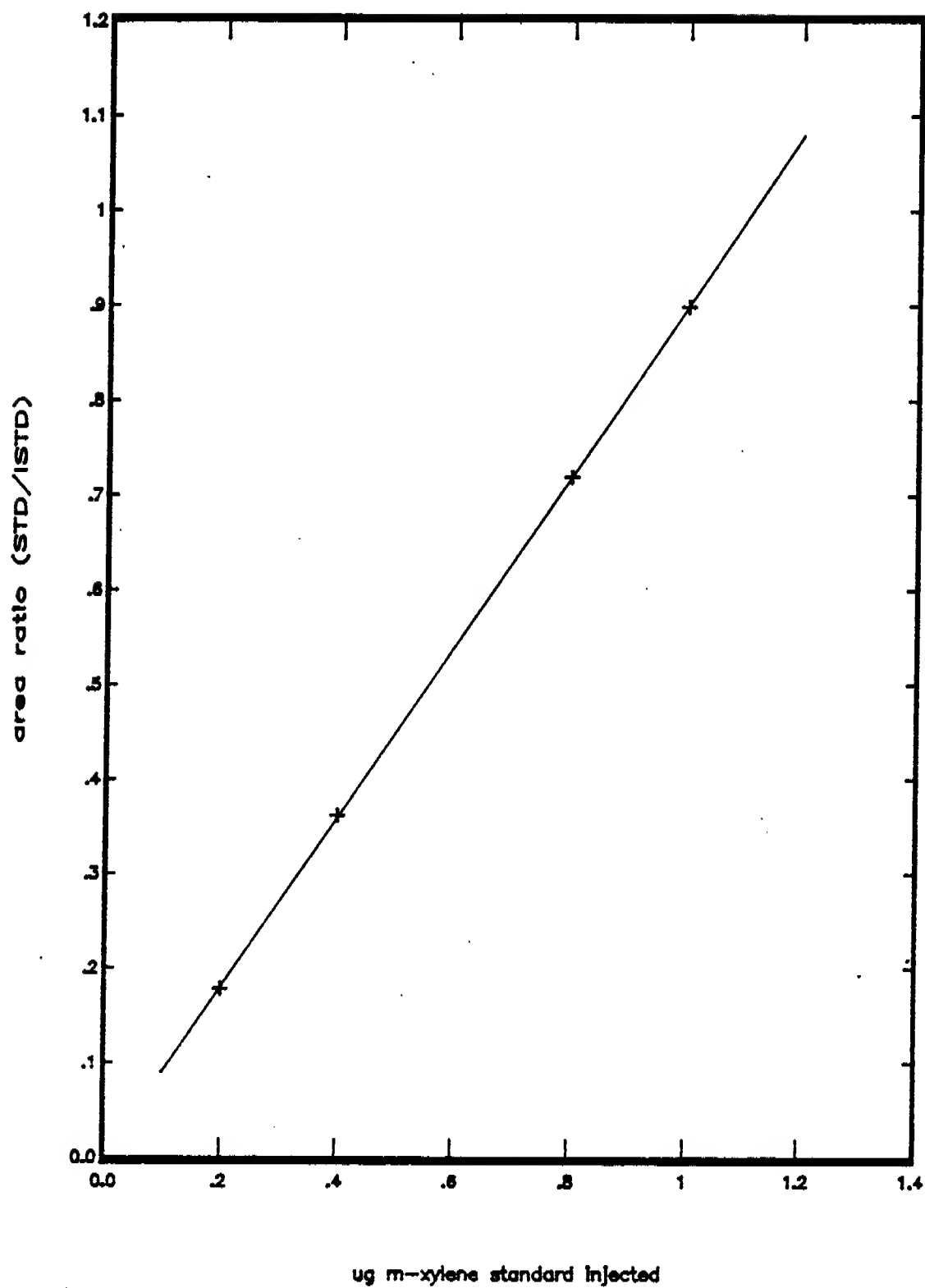
START AUTO SEQ



[-P] 5880A SAMPLER INJECTION @ 19:45 APR 17, 1986

SAMPLE #: ID CODE :

FIGURE 2 - STANDARD CURVE
m-xylene



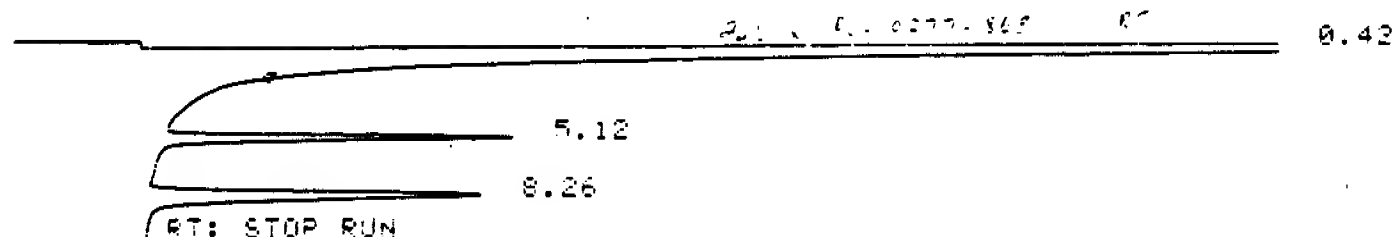
RT EXP RT AREA TYPE WIDTH CAL AMOUNT NAME

0.00 BASELINE @ START RUN = 7.04
 0.00 THRESHOLD @ START RUN = 4
 0.00 PEAK WIDTH @ START RUN = 0.08

RT	EXP RT	AREA	TYPE	WIDTH	CAL	AMOUNT	NAME
5.12	5.12	2608.91	BB	0.288	1	0.786	M-XYLENE
8.26	8.26	3716.91 +	BB	0.430	2	ISTD 1	PROPYLBENZEN

MULTIPLIER = 1
 ISTD 1 AMT = 1

FIG 3 , TYPICAL CHROMATOGRAMS, SAMPLES .



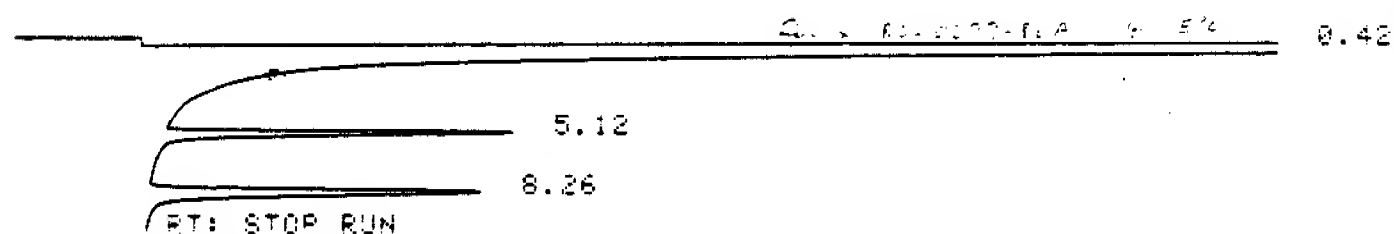
【#】 53804 SAMPLER INJECTION @ 18:58 APR 17, 1986

SAMPLE # : ID CODE :

PROJ. 2399-108 DAY 14 STAB AT RT & SDEC
 ISTD

RT	EXP RT	AREA	TYPE	WIDTH	CAL	AMOUNT	NAME
0.00							
0.00							
0.00							
5.12	5.12	2621.22	BB	0.288	1	0.787	M-XYLENE
8.26	8.26	3728.72 +	BB	0.430	2	ISTD 1	PROPYLBENZEN

MULTIPLIER = 1
 ISTD 1 AMT = 1



【#】 53804 SAMPLER INJECTION @ 19:10 APR 17, 1986

SAMPLE # : ID CODE :

PROJ. 2399-108 DAY 14 STAB AT RT & SDEC
 ISTD

RT	EXP RT	AREA	TYPE	WIDTH	CAL	AMOUNT	NAME
0.00							
0.00							
0.00							
5.12	5.12	2611.95	BB	0.287	1	0.784	M-XYLENE
8.26	8.26	3729.92 +	BB	0.430	2	ISTD 1	PROPYLBENZEN

MULTIPLIER = 1
 ISTD 1 AMT = 1



7. Analysis of Corn Oil for Peroxide

a. Any batch of corn oil used in the Bioassay Program will be analyzed for peroxides before it is first used and at monthly intervals thereafter, while it is in use. Corn oil must be purchased in batches no smaller than 2 gallons (7 Kg) per chemical for which it is the dose vehicle, unless substantially less than this quantity is being used monthly. All corn oil must be stored at 5° C or lower.

b. The following is a standard analytical procedure which can be used for these analyses. The method employed is the Official Method Cd. 8-53 of the A.O.C.S. (1972).^{1/} It determines all substances, in terms of milliequivalents (meq) of peroxide per 1,000 grams of sample, which oxidize aqueous iodide under the conditions of the test. These are

^{1/} Official and Tentative Methods of the American Oil Chemists' Society, 3rd Ed. Revised; V.C. Mehlenbacher, T.H. Hopper, E.M. Sallee, and W.E. Link, Eds., American Oil Chemists' Society, Champaign, Illinois (1972).

This is a contractually specified method.

Notes. 1) Boil and cool all H₂O.

2) Prepare 0.005 N Thio-sulfate by dilution of a commercial standardized thio-sulfate titrant of greater normality

Jerry L. Fitzgerald 5/26/51

Tracor Jitco

generally assumed to be peroxides or other similar products of fat oxidation. The method is highly empirical, and any variation in procedure may affect the results.

c. A 5.0 gram sample of the corn oil to be analyzed is quantitatively transferred into a 250 ml titration flask and 30 ml of glacial acetic acid:chloroform (60:40 v/v) is added. The mixture is stirred until the corn oil has completely dissolved. One-half milliliter of a saturated aqueous potassium iodide solution is added. The test solution is stirred thoroughly and allowed to stand for exactly 1 minute, after which 30 ml of distilled water is added. The iodine liberated by the peroxides in this solution is titrated potentiometrically with standard 0.005 N sodium thiosulfate solution, stirring vigorously to ensure thorough mixing. An automatic titrator with platinum disk working electrode and silver - silver chloride reference electrode is convenient. Titrations should be run in triplicate. A blank titration of reagents should be run on the day the oil sample is analyzed; the blank should not titrate more than 1.0 ml of the 0.005 N sodium thiosulfate standard solution. Peroxide number, expressed in milliequivalents of peroxide per kilogram of oil (meq/kg), is calculated as follows:

$$\text{Peroxide Number} = \frac{(V - B) \times N \times 1,000}{W}$$

V = volume (in ml) of thiosulfate solution required for titration of oil sample

B = volume (in ml) of thiosulfate solution required for titration of reagent blank

N = normality of sodium thiosulfate solution

W = Weight of oil sample in grams

d. Results should be reported as shown in Figure 13 to this Attachment A. In this report, the method above can be cited by reference to this document, but the instrument used for the titration must be specified. When reporting follow-up analyses, the dates and results of all previous analyses of the batch should be included for comparison. Conclusions and actions taken as a result must be noted, and the report must be signed and dated by the responsible chemist. These reports should accompany the first Monthly Progress Report after the analysis.

e. Corn oil with a peroxide number equal to or less greater than 10 meq/kg will be considered rancid for purposes of this program and must be replaced immediately.

Footnotes:

(61A) Changed 10/26/79 by Modification 70

Dist. G. Wolfe, I. Foxx, M. Rodwin, Project File

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioassay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Duke's Pure Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 5K21

Additives (if known): Not indicated

Date procured: 1/14/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical Method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination electrode (platinum/AG/AgCl), Fisher Cat. No. 13-639-82.

<u>Date of Analysis</u>	<u>Peroxide Number (from each individual titration, meq/kg)</u>	<u>Average Peroxide Number (meq/kg)</u>
4/21/86	1.11, 1.07, 1.04	1.07 ± 0.035 S.D.

Previous Analyses

1/31/86	0.611, 0.616, 0.611	0.613 ± 0.003 S.D.
3/03/86	0.893, 0.888, 0.892	0.891 ± 0.003 S.D.

Conclusions: Peroxide number is well below the limit of 10 meq/kg.

Signed
Date

Lee Hahnig
5-16-86

Approved

Susan A. Lewis

Dist. G. Wolfe, J. Fox, M. Rodwin, Project File

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioassay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Schneck's Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 775

Additives (if known): Not indicated

Date procured: 5/15/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination electrode (platinum/AG/AgCl), Fisher Cat. No. 13-639-82.

<u>Date of Analysis</u>	<u>Peroxide Number (from each individual titration, meq/kg)</u>	<u>Average Peroxide Number (meq/kg)</u>
5/19/86	1.14, 1.14, 1.13	1.14 ± 0.006 S.D.

Previous Analyses

Conclusions: Peroxide number is well below the limit of 10 meq/kg.

Signed
Date

Lee Hakway
5-20-86

Approved

James L. Stuckman

Dist. L. Wolfe, I. Foxx, M. Rodwin, Project File

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioassay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Schneck's Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 775

Additives (if known): Not indicated

Date procured: 6/20/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination electrode (platinum/AG/AgCl), Fisher Cat. No. 13-639-82.

<u>Date of Analysis</u>	<u>Peroxide Number (from each individual titration, meq/kg)</u>	<u>Average Peroxide Number (meq/kg)</u>
6/20/86	1.37, 1.37, 1.37	1.37 ± 0.00 S.D.
<u>Previous Analyses</u>		
5/19/86	1.14, 1.14, 1.13	1.14 ± 0.006 S.D.

Conclusions: Peroxide number is well below the limit of 10 meq/kg.

Signed
Date

Lee Hocking
6-23-86

Approved

James L. Donkner

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioassay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Schneck's Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 775

Additives (if known): Not indicated

Date procured: 6/20/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination electrode (platinum/AG/AgCl), Fisher Cat. No. 13-639-82

<u>Date of Analysis</u>	<u>Peroxide Number (from each individual titration meq/kg)</u>	<u>Average Peroxide Number (meq/kg)</u>
7/17/86	1.63, 1.64, 1.63	1.63 ± 0.006 S.D.

Previous Analyses

5/19/86	1.14, 1.14, 1.13	1.14 ± 0.006 S.D.
6/20/86	1.37, 1.37, 1.37	1.37 ± 0.00 S.D.

Conclusions: Peroxide number is well below the limit of 10 meq/kg.

Signed Kee Habung
Date 7-18-86

Approved Susan A. Harris



HAZLETON

LABORATORIES AMERICA, INC.

1330 - 8 PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

ATTACHMENT B

Chemical Characterization of the Test Material:

1. Report of Analysis, Hazleton Laboratories America, Madison, Wisconsin.
 - a - Moisture, Karl Fischer method
 - b - GC purity
 - c - IR spectra
 - d - GCMS
 - e - NMR
2. Elemental analysis, Micro-Tech Laboratories, Inc., Skokie, Illinois.
3. Report of Analysis, Hazleton Laboratories America, Madison, Wisconsin.
 - a - Final GC purity

**HAZLETON**

LABORATORIES AMERICA, INC.

Chemical & BioMedical Sciences Division

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- 416 -

REPORT OF ANALYSIS

LEE HOHING
HAZLETON BIOTECHNOLOGIES CORPORATION
9200 LEESBURG TURNPIKE
VIENNA, VA 22180

SAMPLE NUMBER: 60302711

DATE ENTERED: 03/13/86

REPORT PRINTED: 04/30/86

M-XYLENE (RO-0218 86)

PURCHASE ORDER NUMBER: 002107

ASSAY
MOISTURE, KARL FISCHER METHOD

<u>ANALYSIS</u>	<u>UNITS</u>
.173	%

G.C. PURITY

PURITY BY G.C. ANALYSIS

99.1	%
------	---

METHOD REFERENCE

HAZLETON LABORATORY WORKSHEET 05XX 000166-00.

IR SPECTRA

EXHIBITS CHARACTERISTIC PEAKS FOR THIS COMPOUND

METHOD REFERENCE

ALDRICH REFERENCE BOOK OF IR SPECTRA.

GCMS

REPORT TO BE GENERATED MANUALLY

NMR

REPORT TO BE GENERATED MANUALLY

CARBON	86.51	%
HYDROGEN	9.38	%
OXYGEN	0.35	%

METHOD REFERENCE

ANALYSIS PERFORMED BY MICRO-TECH LABORATORIES, INC., SKOKIE, IL



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- 417 -

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SAMPLE NUMBER: 60302710

PAGE 2

M-XYLENE (RD-0218 86)

METHOD REFERENCES

MOISTURE, KARL FISCHER METHOD
UNITED STATES PHARMACOPEIA, VOLUME XX, PAGE 988 (1980).

METHOD LISTED ABOVE WITH RESULTS

GCMS
METHOD PER ANALYSIS



THE UNIVERSITY OF WISCONSIN-MILWAUKEE/P.O. Box 413, Milwaukee, Wisconsin 53201

COLLEGE OF LETTERS AND SCIENCE
DEPARTMENT OF CHEMISTRY

PHONE: (414) 963-4411

To: Joe Polywacz
Hazleton Laboratories

From: James Otvos, Asst. Professor *J. Otvos*

Re: NMR analysis of LIMS #'s 60301753-60301754 and
60302709-60302711 *HLA-VA*

Date: April 21, 1986

Enclosed are ^1H NMR spectra of p-xylene(60302709), m-xylene(60302710), and o-xylene(60301754) in deuteriochloroform solvent which positively confirm their identities. The o-xylene sample was labeled "o-xylol", but is in fact xylene. An unexpected peak at 2.21 ppm was found in the p-xylene sample which was attributed to a solvent contaminant (probably H_2O) since a ^{13}C NMR spectrum of the same sample failed to exhibit any extra resonances. The three xylene samples are at least 98% pure as judged by the intensities of several small resonances of unknown origin in the spectra.

^{13}C spectra were taken of the remaining two samples, strychnine (60301753) and brucine(60302711), because they are much more diagnostic of the structures of these compounds compared to ^1H spectra. As the enclosed spectra indicate, the samples are pure. The number of resonances observed in each spectrum and their chemical shifts confirm the identities of the two compounds.

4117 OAKTON STREET

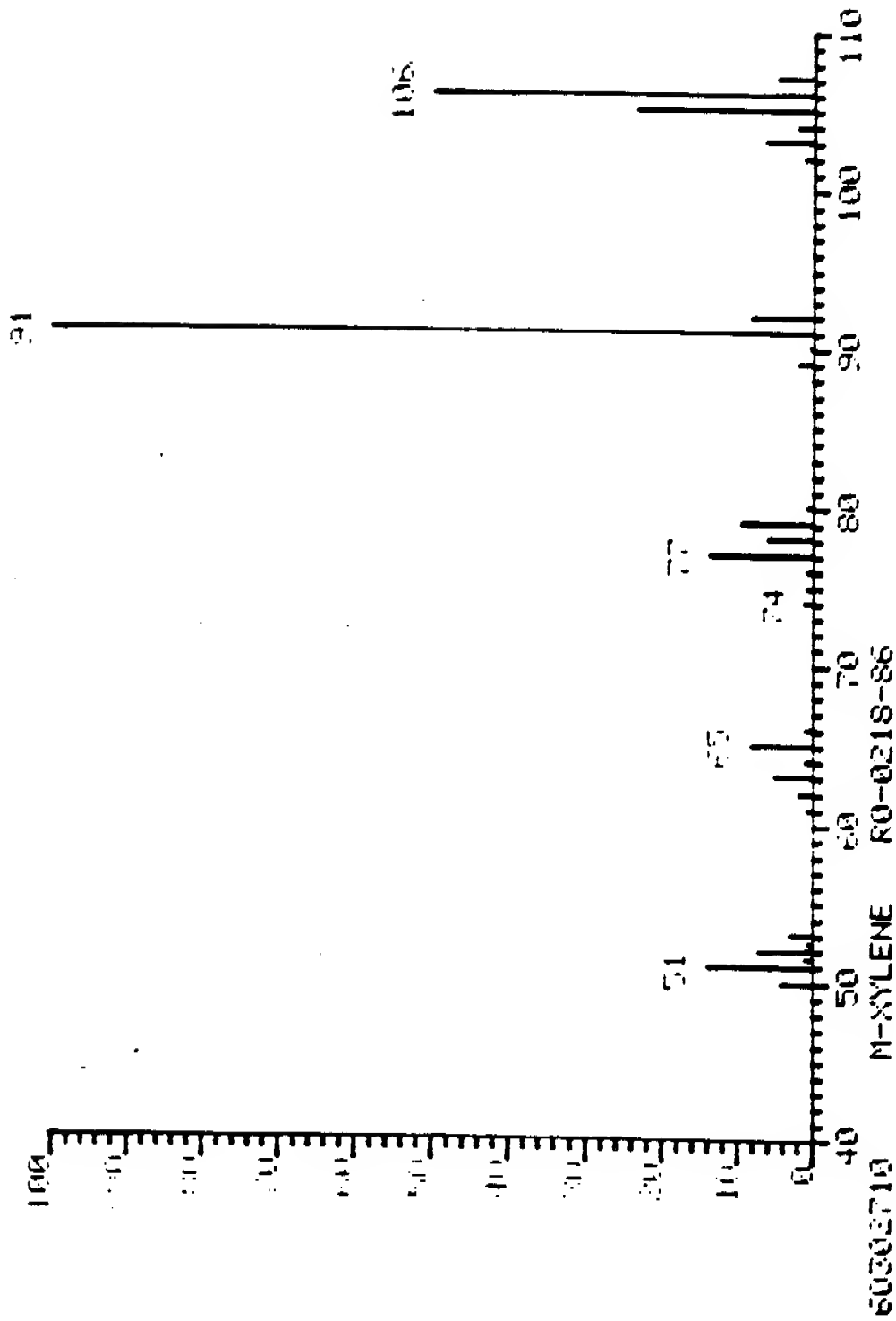
SKOKIE, ILLINOIS 60076

April 10, 1986

[illegible]

Very truly yours,

June B. Gast



60302710 M-XYLENE R0-0218-86

ANALYSIS NAME: HZLE.DAT;S SPEC# 17 NORM: 6 /SCALE: 41230

PL# DATE: APR 2 86 13:16:51 U03.6

Analyzed 3/21/86
[Signature]

GSX: SLIST OF HH00:1007,300JHZLE.DAT;5
APR 2 86 13:16:34 VERSION V03.6

60302710 m-xylene RC-0218-86
PAGE: 1

SPECTRUM NUMBER: 17

NUMBER OF PEAKS: 31

NORM. FACTORS: 1. 412.20

Analyzed 3/2/86
W. J. M.

PEAK#	MASS	A	B
1	49.9	1696.	4.11
2	51.0	5708.	13.85
3	51.6	376.	0.91
4	52.0	2916.	7.07
5	52.1	360.	0.87
6	52.6	240.	0.58
7	53.1	1216.	2.95
8	61.1	276.	0.67
9	62.1	788.	1.91
10	63.1	2108.	5.11
11	64.1	408.	0.99
12	65.1	3404.	8.26
13	66.1	396.	0.96
14	74.1	448.	1.09
15	75.0	296.	0.72
16	76.1	336.	0.82
17	77.1	5604.	13.60
18	78.1	2448.	5.94
19	79.1	3912.	9.49
20	80.1	288.	0.70
21	89.1	772.	1.87
22	90.1	152.	0.37
23	91.1	41220.	100.00
24	92.1	3356.	8.14
25	102.1	484.	1.17
26	103.1	2628.	6.38
27	103.2	364.	0.88
28	104.1	936.	2.03
29	105.1	9588.	23.26
30	106.1	20524.	49.79
31	107.1	1960.	4.75

***** SLIST PROCESSING COMPLETE *****

Operator <u>Alfred Hummer</u>	Date <u>3-20-86</u>
Column <u>6'</u>	Detector <u>FID</u>
Inn. <u>2 mm</u>	Range <u>51.8</u>
Temp <u>SP1200/Beebe 34</u>	Atm. <u>293</u>
Flow <u>5/175</u>	Flow Rate (ml/min) <u>30</u>
Split <u>Split cap</u>	Flow Rate (ml/min) <u>330</u>
Flow <u>100/100</u>	Flow Rate (ml/min) <u>NA</u>
Carrier Gas <u>Helium</u>	Flow Rate (ml/min) <u>NA</u>
Detector <u>42</u>	Flow Rate (ml/min) <u>100</u>
Inlet Press. <u>380</u>	Flow Rate (ml/min) <u>75</u>
Rate <u>40</u>	Flow Rate (ml/min) <u>75</u>
CHART SPEED <u>Low</u>	Rate <u>NA</u>
SAMPLE <u>M-xylene</u>	Solute <u>Ethyl Ether</u>
Size <u>1ml</u>	Solute <u>neat, dilution</u>

Sample No. <u>NA</u>	Sample Name <u>0540</u>
Sample No. <u>WS 171</u>	Sample Name <u>3-21-86</u>
Analyst <u>MRS</u>	Sample Name <u>3-21-86</u>
Analysis technique <input checked="" type="checkbox"/> <u>X</u>	
Prep No. <u>NA</u>	Prep No. <u>NA</u>
Recorder No. <u>3-90-13</u>	Recorder No. <u>5890A</u>
Channel No. <u>NA</u>	Channel No. <u>NA</u>
Sample No. <u>60302710</u>	Sample No. <u>0540 WS 171</u>
	Sample Name <u>M-xylene</u>

10 9 8 7 6 5 4 3 2 1 0

10 9 8 7 6 5 4 3 2 1 0

6030270 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd

0.0000
0.0000
0.0000

10 9 8 7 6 5 4 3 2 1 0

6030270 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd 2nd

Study No. NA Assay Method(s) OSX
 AP 002 WS 171 Extracted by/date NA 3-20-86
 BY NA NA Calculated by/date NA 3-21-86
 Assay date of sample 3-20-86 OK to 1000 standardization

Pump No. NA NA NA
 Recorder No. 3373 5890 A NA
 Channel No. NA NA NA
 Sample No. 60302710 WS 171 NA
OSX WS 171 m-Xylene

Operator Sheng Shumway Date 7-20-84
 Detector FID
 Range 200
 Atten. 20
 Flow Rates ml/min.
 Hydrogen 30 Air 330
 Nitrogen NA
 Carrier Gas Helium
 Inlet Temp. 100
 Inlet Pressure 3.0 psi
 Column Initial 75
 Column Final 75
 Rate 40 ml/min
 CHART SPEED 0-2
 SAMPLE m-Xylene
 Size 1 ul
 Solvent Went
 Detector check

* RUN # 65 MAR 20, 1986 11:33:03

START

0.680 0.329

1.869

4.254

10.153

STOP

RUN# 65 MAR 20, 1986 11:33:03

AREA2

RT	AREA	TYPE	WIDTH	AREA2
.320	538620160	SPB	.028	94.79933
4.254	29548672	BB	.178	5.20068

TOTAL AREA=5.6817E+08

MUL FACTOR=1.0000E+00

* RUN # 66 MAR 20, 1986 11:46:47

START

0.680 0.321

4.243

4.879

STOP

RUN# 66 MAR 20, 1986 11:46:47

AREA2

RT	AREA	TYPE	WIDTH	AREA2
.321	547633440	SHB	.035	99.81142
4.243	5468842	PB	.177	.98253

TOTAL AREA=5.5312E+08

MUL FACTOR=1.0000E+00

* RUN # 67 MAR 20, 1986 11:54:54

START

0.680 0.000

1.869

2.940

0.680

5.000 5.000

0.000

TOTAL AREA=5.6817E+08
MUL FACTOR=1.0000E+00

* RUN # 66 MAR 20, 1986 11:46:47
START

0.680 0.321

4.879 4.243

4.879

STOP

RUN# 66 MAR 20, 1986 11:46:47

AREA#

RT	AREA TYPE	WIDTH	AREA#
.321	547653448 SHB	.035	99.81142
4.243	5468842 PB	.177	.99853

TOTAL AREA=5.5312E+08
MUL FACTOR=1.0000E+00

* RUN # 67 MAR 20, 1986 11:54:54
START

1.165

1.913

2.940

3.650

5.335 5.082

8.285

10.309

11.379

STOP

RUN# 67 MAR 20, 1986 11:54:54

AREA#

RT	AREA TYPE	WIDTH	AREA#
.365	14409872 PB	.028	.51699
1.913	411378 VB	.134	.01476
5.082	2.763E+09 VV	.624	99.12827
5.335	8494771 VV	.164	.08479
10.309	325485 BV	.097	.00221

TOTAL AREA=2.7871E+09
MUL FACTOR=1.0000E+00

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Chemical & BioMedical Sciences Division

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REPORT OF ANALYSIS

LEE HOHING
HAZLETON BIOTECHNOLOGIES CORPORATION
9200 LEESBURG TURNPIKE
VIENNA, VA 22180

SAMPLE NUMBER: 6070623

DATE ENTERED: 07/30/8

REPORT PRINTED: 10/29/8

M-XYLENE: RO-0311-86 REFERENCE CHEMICAL

FINAL PURITY

PURCHASE ORDER NUMBER: 0A12550

SEE ATTACHED CHROMATOGRAMS

METHOD REFERENCES

METHOD LISTED ABOVE WITH RESULTS

**HAZLETON**

LABORATORIES AMERICA, INC.

Chemical & BioMedical Sciences Division

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 703956 HAZRAL MDS UD

REPORT OF ANALYSIS

LEE HOHING
HAZLETON BIOTECHNOLOGIES CORPORATION
9200 LEESBURG TURNPIKE
VIENNA, VA 22180

SAMPLE NUMBER: 6070623

DATE ENTERED: 07/30/8

REPORT PRINTED: 10/29/8

M-XYLENE: R0-0926-86

*BULK chemical
FINAL PURITY*

PURCHASE ORDER NUMBER: 0A12550

SEE ATTACHED CHROMATOGRAMS

METHOD REFERENCES

METHOD LISTED ABOVE WITH RESULTS

Study No(s)	NA		Accty. Information	OSKX
Attached to	NA			
Issued by	LA	JIA 0-28-K		
Analysis technique	NA			
Pump No.	NA	NA	NA	
Recorder No.	NA	08000052	NA	
Channel No.	NA	NA	NA	
Sample No.				

Operator	JH Strosch		Date	10-28-FL
Column	6'	Detector	FID	
Length	2 mm	Range	100	
Phase	SP1200/Bentone 3+	Atten.	4	
Flow Rate	5/1.25	Flow Rates, ml/min.		
Port	Sup. Helicopart	Hydrogen	50	Air 200
Flash	100/120	Solvents		
Carrier Gas	Helium	Split		
Rotameter	22	Temperature °C		
Inlet Press		Pre 100	Inj 100	
Rate	40	Column Inlet	25	
CHART SPEED	low 0.5	Rate	NA	
SAMPLE	M-XYLENE, P-XYLENE	Subst.	6-TMPL 2-TMPL	
Size	1 µl	Dilution		

60706238

60706239

60706242

60706243

60306237 Run = 2, 1st of 0.01 sec in sphere in 1st 21mg 21mg JCA 10-23-86

manjection JCA 10-23-86

60306238 Run = 1, 1st of 0.02 sec in sphere in 1st 21mg JCA 10-23-86



HAZLETON

LABORATORIES AMERICA, INC.

1330 - B PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

HLA 2399-108

- 431 -

APPENDIX 10

Study Protocol and Amendments



HAZLETON
LABORATORIES AMERICA, INC.

1330 - B PICCARD DRIVE.
ROCKVILLE, MARYLAND 20850

PROJECT NO. 2399-108 DATE ISSUED April 7, 1986

PROPOSAL NO. 5-580 STUDY TITLE: Subchronic Toxicity in Rats

TEST MATERIAL (s): Safety, storage, and descriptive information is attached.

- A. Identification m-Xylol (m-Xylene)
B. Lot No. (s) 259211 286
C. Receipt Date March 6, 1986
D. LH Number (s) 10,031A

STUDY LOCATION:
Rockville

PROPOSED INITIATION DATE: April 11, 1986
PROPOSED COMPLETION OF
IN-LIFE PHASE DATE: July 10, 1986

DISTRIBUTION: ORIGINAL SIGNED PROTOCOL TO PSO

FIXED DISTRIBUTION: (No. Copies)*

PERFORMING DEPARTMENTS (~~# copies each Director~~)

Health Services (1) Quality Assurance (1)
Compound Prep (Tox) (1) Contracts (1)
Scientific Res. (Tox) (1) Client Services (1)
Lab Animal Medicine (1) Sponsor (1)

Toxicology (2) Analytical Chemistry (1)

Pathology (4)

* Unless otherwise directed.

Protocol is Attached.

Date and Means of Sponsor Authorization:

Signed protocols to be forwarded by sponsor.

This protocol issued to permit scheduling of the study by the laboratory.

STUDY DIRECTOR: Gary W. Wolfe, Ph.D., D.A.B.T.

DATE: 4/9/86



PROTOCOL

Project No. 2399-108

1. Study Subchronic Toxicity Study in Rats
2. Purpose To evaluate the subchronic toxicity of a test material when administered daily via oral gavage to rats for 90 days.
3. Study Location Hazleton Laboratories America, Inc.
1330-B Piccard Drive
Rockville, Maryland 20850
4. Sponsor and Address Dynamac Corporation
11140 Rockville Pike
Rockville, Maryland 20852
5. HLA Study Director Gary W. Wolfe, Ph.D., D.A.B.T.
6. HLA Study Coordinator Marcia P. Rodwin, B.A.
7. Regulatory Compliance This study is subject to applicable regulations of the Environmental Protection Agency and will be conducted per EPA Pesticide Assessment Guidelines, Subdivision F, Section 158.82-1, Toxic Substances Control Act (TSCA) Testing Guidelines for Ninety Day Subchronic Toxicity Studies, 40 CFR 798.2650, and in accordance with the Good Laboratory Practice Standards, 40 CFR Part 160.
8. Quality Assurance The protocol, in-life phase, interim report and the final report will be audited by Quality Assurance in accordance with standard operating procedures at Hazleton Laboratories.
9. Proposed Study Timetable
Initiation: - April 11, 1986
Terminal Sacrifice: July 10, 1986
Final Report: September 5, 1986



- 2 -

Project No. 2399-108

10. Test Material

- | | |
|--------------------|--|
| A. Identification | m-Xylene (CAS 108-38-3) |
| B. Purity | 99% |
| C. Characteristics | Purity and identity will be determined prior to study initiation, and purity only at termination. (If identity has been established for a 14-day study then only purity needs to be determined prior to start of 90-day study.) |
| D. Reserve Samples | Reserve samples (4 x 10 g) of the test and control articles will be taken at initiation and retained frozen. These archived samples of the test article will serve as reference standards for subsequent purity analyses. These samples, as well as any remaining test material, will be discarded upon acceptance of the study results for regulatory purposes (May 8, 1987). |

11. Experimental Design

- | | |
|-----------------------|---|
| A. Animals | |
| (1) Species | Rat |
| (2) Strain/Source | Sprague-Dawley/Charles River |
| (3) Age at Initiation | Preferably before 6 weeks of age, but not more than 8 weeks of age. |
| (4) Number/Sex | 80/sex |
| (5) Identification | Individual ear tags |
| (6) Husbandry | |
| (a) Housing | Individual |



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- 3 -

Project No. 2399-108

- (b) Food Purina Certified Rodent Chow® 5002, ad libitum. Feed is analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, organophosphates, and specified nutrients. (See Attachment #1 for details).
- (c) Water Acidified water, ad libitum. Water is analyzed twice per year for contaminants as listed in the EPA drinking water standards.
- (d) Contaminants The study director and/or the sponsor have considered possible interfering substances potentially present in animal feed and water, including the test material itself or possible structurally related materials as well as the items listed in (b) and (c) above. None of these contaminants are reasonably expected to be present in animal feed or water at levels sufficient to interfere with this study.
- (e) Environment Every attempt will be made to maintain temperatures at 69 - 78°F with a relative humidity of 50 ± 20%. A 12-hour light/12-hour dark cycle will be maintained. Temperature and humidity will be recorded twice daily.
- (f) Quarantine Approximately two weeks. Animals selected for study will have been determined to be acceptable for admission to the study.
- (7) Randomization Using computer-generated random numbers with assignment to groups. At the time of randomization, the weight variation of the animals of each sex used should not exceed ±2 S.D. of the mean weight, and the mean body weights for each group of each sex will not be statistically different.

(8) Justification

Sprague-Dawley rats historically have been used in safety evaluation studies and are requested by EPA.

B. Group Designation and Dosage Levels

<u>Group No.</u>	<u>No. of Animals</u>		<u>Dosage Levels</u> mg/kg/day
	Male	Female	
1 (Control)	20	20	0
2 (Low)	20	20	100
3 (Mid)	20	20	200
4 (High)	20	20	800

C. Dosing Procedures

(1) Method of
Administration

Oral gavage, 7 days per week for 13 weeks. Treatment will continue until the day before necropsy.

(2) Reason for Dosing
Route

Potential human exposure is by the oral route.

(3) Preparation of Dosing
Formulations

Fresh dosing formulations will be prepared based on stability study. Dosing formulations will be prepared using corn oil and adjusted to 100% compound activity. Dosing factor will be 2.5 ml/kg. Reserve samples from each mixed batch will be retained for possible analysis. These samples will be discarded upon acceptance of the final report.

(4) Analysis of Dosing
Formulations

(a) Stability

Samples of the lowest level will be analyzed at Day 0 and after 7, 14, and 21 days under conditions of use and under refrigeration.

(b) Homogeneity

If the dosage formulation is a suspension, homogeneity of each formulation will be confirmed by analyzing the top, middle, and bottom of each formulation prior to study initiation. If the dosage formulation is a single phase, no homogeneity is required.



- 5 -

Project No. 2399-108

(c) Routine Analyses

Each dosage formulation for weeks 1, 5, 9, and 13 will be analyzed for test material.

(5) Absorption

Though the purpose of this study is not to determine absorption of the test material, toxic or pathologic effects will serve as evidence of absorption.

D. Observation of Animals

(1) Clinical Observations

Twice daily - mortality and morbidity check.

Once daily - cageside observation for obvious indications of a toxic effect, will be recorded about one hour after completion of dosing. In addition, a cursory exam will be conducted while dosing.

Data for specific observations will be recorded on separate forms. Because these are cageside animal checks, the observations will not be as specific as and may not necessarily duplicate those observations recorded on body weight days when thorough physical examinations are conducted.

(2) Physical Examinations

At each weighing interval.

(3) Body Weights

Prior to treatment, at initiation and weekly thereafter.

(4) Food Consumption

Weekly

(5) Ophthalmoscopic Examinations

Prior to treatment and during week 13 using indirect ophthalmoscopy on the last ten animals per sex per group.

E. Clinical Pathology

(1) Frequency

Prior to initiation and during weeks 4 and 13.



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- 6 -

Project No. 2399-108

Blood will be collected via orbital sinus with CO₂ anesthetization.

(2) Number of Animals

(a) Prior to initiation

5/sex randomly selected from animals acceptable for study but not used on study.

(b) During Weeks 4 and 13

10/sex/group (sampled per SOP)

(3) Tests

(a) Hematology

leukocyte count
erythrocyte count
hemoglobin
hematocrit
platelet count
differential leukocyte count
reticulocyte count

(b) Blood Chemistry

sodium
potassium
chloride
total protein
albumin
calcium
phosphorus
total bilirubin
urea nitrogen
creatinine
glucose
SGOT/AST
SGPT/ALT
globulin
alkaline phosphatase
cholesterol
albumin/globulin ratio
LDH



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F. Termination

(1) Unscheduled Sacrifices and Deaths

Necropsies, by trained personnel using procedures approved by board-certified pathologists, will be conducted on all moribund animals and on all animals that die.

(2) Terminal Kill

After 13 weeks of treatment, all surviving animals will be weighed, killed by CO₂ intoxication and subjected to a complete gross necropsy. Necropsies will be conducted by trained personnel under the direct supervision of a board-certified pathologist.

G. Postmortem Procedures

(1) Gross Necropsy

The necropsy will include examination of:

The external surface

All orifices

Cranial cavity

Carcass

External surface of the brain (at necropsy). Cut surfaces of the brain and spinal cord will be examined at the time of tissue trimming.

The thoracic, abdominal and pelvic cavities and their viscera

The tissues and organs of the neck region

Findings will be recorded.

(2) Organ Weights

For each terminally killed animal, the following organs will be weighed following careful dissection and trimming to remove fat and other contiguous tissue in a uniform manner:

liver

kidneys

spleen

adrenals

testes/ovaries

brain

heart



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- 8 -

Project No. 2399-108

(3) Tissue Preservation

The following tissues from each animal will be preserved in 10% neutral buffered formalin:

all gross lesions	kidneys	skin
brain with brainstem	adrenals	epididymis
(medulla/pons, cerebellar cortex, and cerebral cortex)	pancreas	prostate
pituitary	testes	seminal vesicles
thyroid with parathyroids	ovaries	
thymus	uterus	
lungs	spleen	
trachea	aorta	
heart	esophagus	
salivary glands (mandibular)	stomach (forestomach and glandular)	
liver	duodenum, jejunum, ileum	
sternum with bone marrow	colon, cecum, rectum	
mammary gland	urinary bladder	
thigh musculature	mesenteric lymph node	
eyes	sciatic nerve	
	femur including articular surface	
	cervical spinal cord	
	mid-thoracic spinal cord	
	lumbar spinal cord	
	exorbital lacrimal glands	

Electron microscopy will be conducted on livers from control, 200, and 800 mg/kg groups. Detailed methodology will be issued as an amendment to the protocol.

(4) Histopathology

All preserved tissues from all animals will be embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

The following tissues will be examined microscopically:

- (1) All tissues from control and high-dose animals and from all animals not surviving to termination.
- (2) Gross lesions, lungs, liver, and kidneys from all remaining animals.
- (3) Target organs noted at the high-dose level from all animals.



12. Reports

Following termination of the study, a report which includes the following information (as appropriate) will be prepared and submitted:

- Experimental Design and Methods

- Results:

mortality
clinical observations
body weights and
food consumption
clinical pathology tests

ophthalmoscopic findings
organ weights and organ/body
weight ratios
gross pathology
histopathology

- Statistical Analyses:

Statistical methods will be those presented in Attachment #2.

- Statistical Evaluation:

survival rates
growth rates and/or absolute
body weights
total food consumption

clinical pathology values
organ weights and organ/
body weight ratios

- Tables:

mean food consumption values
cumulative survival rates and
mean body weights
summary of clinical
signs for each test group
to include: a list of each
finding and number of
animals affected

summary incidence of
ophthalmoscopic findings
mean clinical pathology values
mean organ weights and organ/
body weight ratios
summary incidence of gross
pathology findings
summary incidence of
histopathology findings



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- 10 -

Project No. 2399-108

- Appendices

week of death for each animal
individual body weights
individual food consumption
individual clinical signs
for each animal to include:
the week of observation of
each sign, a description
of each sign, and its
subsequent course
individual clinical
pathology values

individual ophthalmoscopic
findings
individual organ weights and
organ/body weight ratios
individual gross pathology
findings
individual histopathology
findings
analytical chemistry methods and
results

The final report, or a draft copy of such, will be reviewed by the sponsor within 1 month after receipt. Any revisions or comments will be submitted to Hazleton within this period.

13. Record Retention

All tissue specimens, blocks and slides, and copies of all raw data and the final report will be retained by Hazleton Laboratories. Tissue specimens will be discarded as per work assignment.



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- 11 -

Project No. 2399-108

SIGNATURE PAGE

APPROVED BY:

Hazleton Laboratories America, Inc.:

Gary W. Wolfe
Study Director, Toxicology

Date: 3/14/86

Gary W. Wolfe
Program Manager, Toxicology

Date: 3/14/86

Sponsor:

Sharon G. Angel

4-23-86

• - 2/24/85



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ATTACHMENT #1

CONTAMINANT ANALYSIS FOR CERTIFIED RODENT CHOW[®] 5002 AND WATER

This information identifies the potential contaminants monitored for both laboratory feed and water. The Certified Rodent Chow data are provided by the manufacturer.

1. Certified Rodent Chow[®] 5002 certification profile:

	<u>Maximum Concentration</u>
<u>Heavy Metals</u>	
Arsenic	1.0 ppm
Cadmium	.5 ppm
Lead	1.5 ppm
Mercury	.2 ppm
<u>Aflatoxin</u>	10 ppb
<u>Chlorinated Hydrocarbons and PCB</u>	
Aldrin	.05 ppm
Dieldrin	.05 ppm
Endrin	.05 ppm
Heptachlor	.05 ppm
Heptachlor Epoxide	.05 ppm
Lindane	.05 ppm
Chlordane	.05 ppm
DDT-Related Substances	.15 ppm
PCB	.15 ppm
<u>Organophosphates</u>	
Thimet	.5 ppm
Diazinon	.5 ppm
Disulfaton	.5 ppm
Methyl Parathion	.5 ppm
Malathion	.5 ppm
Parathion	.5 ppm
Thiodan	.5 ppm
Ethion	.5 ppm
Trithion	.5 ppm



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ATTACHMENT #1 (Continued)

2. Standard contaminant analysis for water includes:

Barium	DDE, DDD, DDT
Cadmium	PCB
Chromium	Dieldrin
Copper	BHC
Fluorine	Lindane
Iron	HCB
Lead	Endrin
Manganese	Heptachlor Epoxide
Mercury	2,4-D
Selenium	Silvex (2,4,5-TP)
Sodium	Color Test
Sulfate	Turbidity
Ammonia	Arsenic
Total Nitrogen	Silver
Chloride	Zinc



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ATTACHMENT #2

Analysis of Data

If appropriate, cumulative survival will be analyzed using the National Cancer Institute Package. Trend analysis of survival will be evaluated at the 5.0% one-tailed probability level. Control vs. test group comparisons of survival will be evaluated at the 5.0% one-tailed probability level if trend analysis is significant or at the 5.0% two-tailed probability level if trend analysis is not significant.

Growth rates and other data will be analyzed in the order presented in the flowchart. Tests for homogeneity of variances, ANOVA and the Terpstra-Jonckheere Nonparametric Test for Trend will be evaluated at the 5.0% one-tailed probability level.



ATTACHMENT #3

Protocol Addendum

ANALYTICAL CHEMISTRY

Introduction

The purpose of this work is to provide chemical support for the bioassay studies. This support consists of purity, identity and stability of the bulk compound and development of a method to determine the concentration stability and homogeneity (when indicated) in the dosing vehicle. If the dosing vehicle is corn oil, determination of peroxides in the corn oil will be carried out.

Chemical Characterization of Test Article

The physical appearance will be noted and the source of the chemical together with the manufacturer's stated purity will be reported. The following spectral techniques will be employed initially: Infrared (IR), nuclear magnetic resonance (NMR) and mass spectrometry (MS). Spectra obtained will be compared to literature references¹ and consistency to expected structure. Elemental analysis and determination of water using the Karl Fischer technique will be carried out. A gas chromatographic (GC) technique will be used to assess purity and compared, whenever possible, to known reference standards, if available. Reference samples will be taken on receipt of chemicals and stored frozen for future reanalysis. The GC scan for purity will be carried out and compared to the reserve sample after 4 months (or on receipt of chemical, at the end of the 14-day study and at the end of the 90-day study if more than 4 months have elapsed). Thus, the integrity of and purity of the test article throughout the study will be documented. It is important to choose a GC column that will effectively separate the o-, m- & p-isomers (see Methodology).

Determination of the Test Article in the Dosing Vehicle

Method Validation

A four-point standard curve will be used (excluding 0). Matrix standards and/or spike recoveries will be used if applicable. Imprecision of the low and high standard will be reported as percent relative standard deviation (% RSD) (n=4) and the middle standards will be analyzed twice. The % RSD should be less than 5%. Linear regression analysis will be carried out of the results of the standard curve.

¹Sadtler Standard Spectra, Philadelphia, PA.



ATTACHMENT #3 (Continued)

Prior to the study start, compound preparation will mix the low and the high dosage groups. These samples will be analyzed on two different days (HBC protocol). The dosing vehicle will be corn oil and hence analysis of the corn oil for peroxides will be conducted monthly.

Homogeneity

If more than one phase is present, duplicate analyses of homogeneity will be conducted at the high and low dosage group on samples taken from the top, middle and bottom of the mix. Homogeneity analyses will be repeated if the size of mix changes.

Stability

Stability of the test article in the dosing vehicle will be established on the low and high dosage groups at days 0, 7, 14, and 21 at two temperatures -- refrigerated and under conditions of use.

Concentration Analysis

Doses will be mixed at least weekly (or more often if indicated by stability data). Samples will be analyzed in duplicate prior to dosing on weeks 1, 5, 9 and 13 of the 90-day study.

Analyses will be repeated by the chemist if the duplicates are greater than 10% apart. If the results are greater than 10% from target the study director will be notified.

Methodology

It is proposed to analyze the samples for m-xylene by GC using a column containing Bentone[®] 34. This has been used for many years to separate the xylenes. A new packing 5% SP-2100 1.75% Bentone 34 can apparently reduce the analysis time by 50% without any loss of resolution. We propose to use a Hewlett-Packard 5880A GC equipped with an autosampler, a microprocessor controlled data module and a flame ionization detector. We propose to use n-propyl benzene as an internal standard.

Reports

A brief interim progress report on chemistry will be issued prior to study start, followed by a more formal format as soon after the start as feasible. Concentration analyses will be reported on HLA/HBC Form 55 -- Analysis Report and Request Form. These reports will be incorporated into the final study report.

PRODUCT DESIGNATION

Xylene

SECTION 1. SOURCE & NOMENCLATURE

MATERIAL SAFETY DATA SHEET

SPONSOR'S NAME		EMERGENCY TELEPHONE NO.	
ADDRESS (Number, Street, City, State, Zip Code)			
MOLECULAR WEIGHT 106.2		CHEMICAL FAMILY Aromatic Hydrocarbon	
CHEMICAL NAME AND SYNONYMS Xylol, Dimethyl benzene		FORMULA $C_6H_4(CH_3)_2$	

(Mixture of ortho, meta and para isomers of Xylene)

SECTION 2. HAZARDOUS INGREDIENTS

BASIC MATERIAL	APPROXIMATE OR MAXIMUM % WT. OR VOL.	ESTABLISHED OSHA STANDARD	LD ₅₀		SPECIES	CONC.
			ORAL	PERCUT.		
Xylene		100 ppm	X		rat	4300 mg, k
		= TLV				
		150 ppm				
		= STEL*				
* STEL = Short Term Exposure Limit -						
the max. allowable conc. not to be exceeded						
at any time during the 15 min. excursion limit						

For m. Xylene:

SECTION 3. PHYSICAL DATA

Meta is the major component of commercial Xylene

BOILING POINT (°F) 282° F	VAPOR PRESSURE (mm Hg.) 10 mm @ 28.3° C
MELTING POINT (°F) -54° F	VAPOR DENSITY (Air=1) 3.66
SPECIFIC GRAVITY (H ₂ O=1) 0.87	EVAPORATION RATE (_____ =1)
SOLUBILITY IN WATER (Pts/100 pts H ₂ O) Insoluble	VOLATILE % Vol. % Wt.
APPEARANCE Clear liquid AND ODOR Similar to benzene and toluene	SOLVENTS Organic solv.

SECTION 4. FIRE & EXPLOSION HAZARD DATA

FLASH POINT METHOD USED 84° F	Ignition temperture: 982° F	FLAMMABLE (EXPLOSIVE) LIMITS	UPPER 7.0 LOWER 1.1
EXTINGUISHING MEDIA Use Dry Chemical. Water maybe ineffective because of low flash point			
SPECIAL FIRE FIGHTING PROCEDURES Wear full-face mask self-contained breathing apparatus which provides eye protection.			
UNUSUAL FIRE AND EXPLOSION HAZARDS Material can be ignited under almost all normal temperature conditions. Vapors form explosive mixtures in air. Avoid flame, heat, sparks. Vapor may travel a considerable distance to a source of ignition and flash back.			

MATERIAL SAFETY DATA SHEET

SECTION I

Manufacturer's Name _____ Emergency Phone No. _____
 Address (No., Street, City, State, Zip Code) _____

Chemical Name and Synonyms Xylene Trade Name and Synonyms _____
 (Xylol, Ethyl Benzene)
 Chemical Family Aromatic Hydrocarbon Formula $C_6H_4(CH_3)_2$
 may be mixture of O-, M-, and P-Xylenes

SECTION II HAZARDOUS INGREDIENTS

Paints, Preservatives, & Solvents	%	TLV (Units)	Alloys and Metallic Coatings	%	TLV (Units)
Pigments			Base Metal		
Catalyst			Alloys		
Vehicle			Metallic Coatings		
Solvents			Filler Metal plus Coating or Core Flux		
Additives			Others		
Others					
Hazardous Mixtures of Other Liquids, Solids and Gases				%	TLV (Units)

SECTION III PHYSICAL DATA

Boiling Point ($^{\circ}$ F.)	291	Specific Gravity ($H_2O = 1$)	0.9
Vapor Pressure (mm Hg.) 8mm Hg @	72 $^{\circ}$	Percent Volatile By Volume (%)	
Vapor Density (Air = 1)	1.1	Evaporation Rate ($= 1$)	
Solubility in Water	Insol.		
Appearance and Odor			

SECTION IV FIRE AND EXPLOSION HAZARD DATA

Flash Point (Method Used)	81 $^{\circ}$ -90 $^{\circ}$ F	Flammable Limits	Lel	Uel
			1%	7%
Extinguishing Media	Dry chemical, carbon dioxide, foam			
Special Fire Fighting Procedures	Avoid contact with skin, wear self-contained breathing apparatus.			
Fire and Explosion Hazard:				

PRODUCT
DESIGNATION Xylene

SECTION 5. HEALTH HAZARD DATA (IF AVAILABLE)

TOXIC LEVEL	Inhalation - human TCL ₀ *: 200 ppm *TCL ₀ = lowest published toxic con.	CARCINOGENIC	No
PRINCIPAL ROUTES OF ABSORPTION	Lungs	SKIN AND EYE IRRITATION	Skin irritant
RELEVANT SYMPTOMS OF EXPOSURE	Local irritation, CNS excitation and depression. Transient euphoria, headache, giddiness, vertigo, ataxia and tinnitus, confusion.		
EFFECTS OF CHRONIC EXPOSURE	Rabbits chronically exposed developed a decrease in the number of red blood cells and leucocytes and an increase in the platelet count.		
EMERGENCY AND FIRST AID PROCEDURES	Remove from exposure. Wash affected body areas with copious amounts of soap and water. If eye is contaminated, flush with water for at least 15 mins. Notify Medical Office immediately		

SECTION 6. REACTIVITY DATA

CONDITIONS CONTRIBUTING TO INSTABILITY	Normally stable
CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION	None expected
INCOMPATIBILITY (Materials to Avoid)	Avoid oxidizing materials
HAZARDOUS DECOMPOSITION PRODUCTS	None expected

SECTION 7. SPILL OR LEAK PROCEDURES Eliminate all sources of ignition and flammability

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED	Wearing full-face canister gas mask, lab coat, rubber gloves, confine spill, absorb on toweling or bedding and place in impervious container
WASTE DISPOSAL METHOD	Incineration

SECTION 8. SPECIAL PROTECTION INFORMATION

VENTILATION REQUIREMENTS	Transfer operations	PROTECTIVE EQUIPMENT (Specify Types)
LOCAL EXHAUST	Should be done in chemical fume hood.	EYE Goggles
MECHANICAL (General)	Required	GLOVES Rubber gloves (neoprene)
SPECIAL	Inhalation chambers for test system	RESPIRATOR Half-face respirator with cartridge effective against organic vapors.
OTHER PROTECTIVE EQUIPMENT	Lab coat	

SECTION 9. SPECIAL PRECAUTIONS

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORAGE	Protect against physical damage. Outside or detached storage is preferable. Inside storage should be in a standard flammable liquids storage room or cabinet.
OTHER PRECAUTIONS	Separate from oxidizing materials.

Signature <i>Joseph A. Coco</i> <i>Office of Occupational Safety and Health</i>	Date 8/22/77	Address Office of Occupational Safety and Health
---	-----------------	---

SECTION V HEALTH HAZARD DATA

Threshold Limit Value 100 ppm

Effects of Overexposure Irritant to mucous membranes. Gastrointestinal disturbances, skin irritant, erythema, defatting on skin contact, eye irritation at 200 ppm.

Emergency and First Aid Procedures Remove from exposure. Administer oxygen if respiratory distress. Call physician immediately. On skin contact wash with soap and water. Discard wetted clothing.

SECTION VI REACTIVITY DATA

Stability	Unstable		Conditions to Avoid
	Stable	X	

Incompatibility (materials to avoid) Can react with oxidizers

Hazardous Decomposition Products

Hazardous Polymerization	May Occur		Conditions to Avoid
	Will Not Occur	X	

SECTION VII SPILL OR LEAK PROCEDURES

Steps to be taken in case material is released or spilled Confine spill. Absorb on paper or bedding. Place into impervious container.

Waste Disposal Method Incineration

SECTION VIII SPECIAL PROTECTION INFORMATION

Respiratory Protection (Specify type) Half-mask respirator with organic vapor cartridges up to 10X TLV gask mask and conister at higher concentrations.

Ventilation	Local Exhaust Transfer operations in chemical fume hood.	Special
	Mechanical (General)	Other

Protective Gloves Impervious gloves Eye Protection Avoid eye and face contact, wear goggles or face shield.

Other Protective Equipment Protective clothing.

SECTION IX SPECIAL PRECAUTIONS

Precautions to be taken in handling and storing Store in well-ventilated area. Away from heat, arcs.

Other Precautions

PROTOCOL AMENDMENT



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LABORATORIES AMERICA, INC.

1330-B PICCARD DRIVE
ROCKVILLE, MARYLAND 20850

PROJECT NO. 2399-108 AMENDMENT NO. 1 DATE EFFECTIVE: May 20, 1986

STUDY TITLE: Subchronic Toxicity Study in Rats with M-Xylene

DISTRIBUTION: ORIGINAL SIGNED PROTOCOL TO PSO

FIXED DISTRIBUTION: (No. Copies)*

PERFORMING DEPARTMENTS (4 copies each Director*)

Health Services (1)	Quality Assurance (1)
Compound Prep (Tox) (1)	Contracts (1)
Scientific Res. (Tox) (2) (1)	Client Services (1)
Lab Animal Medicine (1)	Sponsor (1)

Toxicology (2) Analytical Chemistry

Pathology (5)

* Unless otherwise directed.

Date and Means of Sponsor Authorization (if appropriate):

Amendment:

Signed protocol forwarded by sponsor (signature page attached).

STUDY DIRECTOR:

Gary W. Wolfe, Ph.D.

DATE:

5/26/86



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LABORATORIES AMERICA, INC.
1330 - B PICCARD DRIVE, ROCKVILLE, MARYLAND 20850

SIGNATURE PAGE

APPROVED BY:

Hazleton Laboratories America, Inc.:

Gary W. Wolfe
Study Director, Toxicology

Date: 3/14/86

Sponsor:

Sharon A. Vogel

4-23-86

Gary W. Wolfe
Program Manager, Toxicology

Date: 3/14/86